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A FOLLOW-UP STUDY OF PERTUSSIS IN INFANCY*

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INJURY to the central nervous system has long been known to be one of the risks of the contagious diseases of childhood, and it has long been suspected that the risk of such accidents was more severe in whooping cough than in the other common diseases, and that children under two years of age have been more frequently affected by the encephalitic complications of whooping cough. It also seems probable that the disease in infancy may, as shown for lead poisoning without convulsions,[1] interfere with subsequent maturation processes in the brain. Finally, since it seems increasingly clear that the disease can be virtually eliminated by the administration of vaccine,[2] though at some risk to the central nervous system, the long-time outlook for infants contracting the disease should be investigated.

Several other observers have attempted to elucidate this problem. Lurie and Levy[3] reported on a group of 58 children who had pertussis under two years, selected from among 500 children seen because of behavior difficulties. Among this group were many who showed neurologic defects, and a high incidence of nerve deafness was a surprising finding. Since the etiologic diagnosis was made in retrospect, the study has been criticized for its conclusions. Levy and Perry[4] investigated a group of 128 inmates of a state home for feebleminded children, who gave a clear history of pertussis, and came to the conclusion that this disease was related to the defect in 15 per cent of the total group. In those who had contracted the disease under two years of age, it appeared to be the cause of the defect in 29 per cent; it seemed responsible for the mental defect in 14 per cent when it occurred between two and five years, and in only 2 per cent when it occurred after five years. These figures suggest that the stage of maturity at the time of attack may be important. Again, this group showed a high incidence of nerve deafness. Baker[5] briefly reviewed the literature and pointed out the much greater frequency and gravity of the encephalitic complications of pertussis as compared to the other common contagious diseases of childhood.

The present study is a follow-up report of 39 children who were admitted to the Children's Hospital, Boston, between the ages of three weeks and two years because of pertussis, with or without complications, during the fourteen-year period January 1, 1931, to December 31, 1944. Eighty-nine other children conforming to our requirements were admitted during this time, but could not be traced for follow-up examination. Of the 39 children studied, 3 appeared to have had cerebral defects prior to their pertussis; 1 had multiple congenital anomalies and was obviously defective prior to pertussis contracted at eighteen months; a second was a 3-pound, 10-ounce, premature baby who had had neonatal convulsions, grossly bloody spinal fluid and generalized rigidity prior to pertussis and was therefore excluded from further consideration; and a third had an occipital encephalocele and was obviously defective prior to his whooping cough at twenty-one months of age. A fourth child had measles with encephalopathy subsequent to that disease three months after the pertussis, and this case was also discarded.

As far as one could tell, the remaining 35 children appeared to be an average group of infants. Their ages at the onset of pertussis varied from twenty-four days to twenty-three months. Of these babies, 23 had uncomplicated whooping cough on admission to the hospital, 8 had complicating pneumonia and 4 had complicating encephalopathy, and of these 1 had both pneumonia and encephalopathy.

The evidence for a diagnosis of pertussis at the time of hospitalization has been discussed by one of us (N.D.R.) in another paper.[6] Suffice it to say here that all patients ran a course of gradually increasing paroxysmal cough that was diagnostically convincing to the hospital staff. Cultures in our hospital have been extremely unreliable, and white-cell counts, unless often repeated, were unreliable.

During the past two years we have interviewed personally all but 2 of the 35 relevant patients, and

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on these 2 we have reports by letter that seem entirely convincing.

Of this total group, 26 had developed normally and were regarded by their families as competent. Fourteen had reached school age and were doing average work or better in grades appropriate to their ages, and of these, 5 were getting honor grades consistently. One of these children had been given pertussis vaccine at eight months of age and had had an average attack of pertussis at nineteen months. Twelve children were still between three and six years of age, but their developmental histories were average. Of these, 1 seemed anxious, but came from an unstable home, 1 was said to be stubborn, and 1 other had temper tantrums. As nearly as could be determined, their behavior problems did not seem unusual. These children were all considered to have recovered without sequelae, although there could be a difference of opinion about one or two of the younger ones.

Among the children who recovered were 2 originally admitted to the hospital because of frank evidences of encephalopathy complicating the pertussis. In addition, 2 children had periods of loss of consciousness after coughing during their hospital stay, and 2 more had repeated convulsions; all 6 have made an apparently satisfactory recovery. The following history is illustrative of a severe encephalitic course with recovery:

Case 1. N. E. M., a healthy 5½-month-old female infant, was admitted to the hospital with a history of exposure to 4 siblings with typical whooping cough. Five days before admission she began to cough. On the day before admission she became listless and would not drink. The temperature rose to 102°F., and the cough became paroxysmal. On the day of admission she could be roused with difficulty and had 2 convulsions, each of about ½ hour's duration.

On admission, the temperature was 102°F.; there were irregular gasping respirations and, fixed staring eyes. The limbs were rigid, with ankle clonus. She did not respond to light, sound or pinprick. There were forceful and obligatory tonic neck reflexes.[7] Constant muscular twitchings appeared around the eyes and mouth.

The white-cell count was 45,700, with 73 per cent lymphocytes. The spinal fluid showed 2 lymphocytes per cubic millimeter and a total protein of 51 mg. per 100 cc. Two nasopharyngeal cultures were negative for *Haemophilus pertussis*.

Because of an x-ray diagnosis of pneumonia, sulfadiazine was given, and two doses of 20 cc. of hyperimmune serum were administered. The patient had many paroxysms of coughing and several convulsions daily for 10 days. Subsequently, the spasticity of the limbs relaxed and by the 18th day she was smiling and responsive and eating well.

She was seen repeatedly during the next 4 years, and her development seemed average and orderly. At the age of 4 years and 9 months a psychologic examination gave average results, showing good attention and persistence in visuomotor, performance and language tests. Her personality adjustment in the family was happy and easygoing.

The final diagnosis was pertussis followed by encephalopathy, with recovery.

Nine of the 35 children had evidence of more prolonged intellectual and emotional difficulties, which in 6 seemed sufficiently severe and persistent to compromise their competitive status. Since generalization about these children seems impossible, their case summaries are presented.

Case 2. H. W. was born at full term of healthy parents, by breech delivery. The birth weight was 6 pounds. There was no family history of mental disease. He cried immediately on delivery and did well during his 5 days' stay in the obstetric hospital. On arrival at home he was exposed to his 4-year-old sister, who had a cough, subsequently running the course of pertussis, with vomiting, whooping and cyanosis. At the age of 3½ weeks the baby contracted a cold, and at 4 weeks he was admitted to the hospital. At that time he was described as alert, with a head of normal contour (no measurements given). He ran a course of severe pertussis with 20 or 30 paroxysms a day, accompanied by severe cyanosis during the 1st weeks. At times he "seemed unconscious" after the paroxysms, but had no convulsions.

The white-cell count was 16,100, with 80 per cent lymphocytes. His weight on admission to the hospital was 7 pounds, and it remained within a few ounces of this figure until 4 weeks after admission, after which he gained a pound in 2 weeks.

He reported to the outpatient department several times in the following year. At 8 months of age (7 months after the onset of the whooping cough), he was thought to be unresponsive, he was unable to sit, and his cranial vault was noted to be small. At 7 years he was leading a wheel-chair life, and had a very small cranial vault, no speech and no sphincter control.

The final diagnosis was microcephalic idiocy, probably due to pertussis.

Case 3. R. L. was the 2nd child of young parents of the laboring class. He was born normally at term and did well until 3 months of age, when he had a fever and rash, thought to be measles by the family. No data about his development were available at 4 months, when he had a cold and a cough and vomiting, and was admitted to the hospital with a paroxysmal cough, temperature of 102°F. and signs of consolidation in the left lower lobe, confirmed by x-ray study.

The white-cell count was 16,200, with 73 per cent lymphocytes. No cultures for *H. pertussis* were made. He had 8 to 10 paroxysms daily, with severe cyanosis and vomiting for 1 week, after which they decreased rapidly. After some of the paroxysms he was noted to be rather stiff, though he had no frank convulsions, and during the first several days he was semicomatose. No lumbar puncture was done. The temperature fell to normal 48 hours after the institution of sulfathiazole therapy. On the 12th day, when he was about to be discharged, chicken pox developed, the temperature being 103°F. for 48 hours, from which he recovered without incident.

His development thereafter was slow in all respects, and at 8 years of age he was admitted to the Wrentham State School for the Feebleminded with an I.Q. of 37.

The final diagnosis was mental deficiency, probably due to pertussis.

Case 4. N. M. was first admitted to the hospital at 2 days of age because of convulsions. At that time she had a cephalhematoma and bloody spinal fluid. She improved rapidly and was seen in the outpatient department several times. Her subsequent development was satisfactory. She stood in her crib at 6 months, walked alone at 12 months, and had one or two conditioned tricks at this time.

Without known exposure, at 14 months of age she contracted a cough, which became paroxysmal, accompanied by cyanosis, vomiting and whooping. During the 3rd week she became unconscious, with fever and convulsions. On admission to the hospital she was cyanotic and semicomatose, and had signs of consolidation at the left base, confirmed by x-ray examination. The convulsions recurred during the first 12 hours in the hospital. She was treated with Luminal Sodium and oxygen, and improved gradually. One cough plate was negative for *H. pertussis*. The white-cell count was 68,300, with 67 per cent lymphocytes. No lumbar puncture was done. Over the next 5 days the temperature subsided and the cough diminished, but she remained unresponsive. On the 18th day after admission she had a recurrence of fever and consolidation in the left side of the chest, this time with a polynuclear leukocytosis. She recovered

gradually and was discharged 35 days after admission, at the age of 16 months.

After discharge from the hospital she had to "learn to walk all over again" and was uninterested in speech, though she seemed to hear. She began to talk soon after she was 2 years old, however. She was held back in the fourth grade for 3 years and then sent to special class. At 12 years of age petit-mal seizures developed. When she was last seen, at 17 years of age, the right pupil was larger than the left. An electroencephalogram showed single large diphasic spikes scattered in all leads. Psychologic examination demonstrated marked irregularity, with fairly adequate responses to concrete situations, but marked impairment of reasoning ability and ability to understand abstract ideas. From the personality point of view she was defiant but easily influenced, and her parents considered her so unreliable as to need permanent protection.

The final diagnosis was mental deficiency due to pertussis.

During this illness the patient's development regressed, and she is, at seventeen years of age, handicapped by intellectual irregularities of a sort often seen after cerebral injury, by petit-mal seizures and by lack of judgment. It is difficult to determine how much of the present difficulty was due to her neonatal difficulty, but the evidence that whooping cough damaged her further seems clear.

Case 5. P. M., an 8-month-old female infant, was first admitted to the hospital because of cough and labored breathing. At this time she was found to have bronchopneumonia and congenital heart disease, for which she had been studied repeatedly, with the evolution of a diagnosis of persistent ostium primum. She had many recurrent respiratory infections. Not much developmental history was available, but she was walking when seen at 17 months and talking at 23 months.

When she was 22 months old her 2 siblings contracted whooping cough, and 2 weeks later she began to cough. At 23 months she was admitted to the hospital with severe uncomplicated pertussis, having many paroxysms per 24 hours. X-ray films showed diffuse mottling of both lungs. The white-cell count was 33,200, with 60 per cent lymphocytes. Cough plates grew no *H. perussis*. She had a temperature of 101 to 102°F. for 5 days and then improved slowly, and was discharged on the 20th day. At no time did she have convulsions, unconsciousness or other evidence of acute encephalopathy during the hospital stay.

Developmental defects were first noted when she began to run into difficulty in school work. She had to repeat two grades. At 17 years of age she was having difficulty in the tenth grade. Psychologic examination showed an I.Q. between 95 and 100, but with great irregularities, especially in the visuomotor sphere, marked reading difficulty and inability to deal with abstractions, such as digits. Her attention spans were short and abstract reasoning was inadequate for her age. From the personality point of view she was fearful, antagonistic and childlike.

The final diagnosis was congenital heart disease with mental irregularities probably due to pertussis.

This patient's progress in school had been difficult because of intellectual and personality difficulties of the sort usually associated with cerebral damage rather than with a congenital defect. Whether the anoxia secondary to her congenital cardiac disease played an important part in the difficulty is hard to say.

Case 6. E. del G. was born at term by forceps delivery, and was breast fed until she contracted whooping cough from her older brother, at 10 weeks of age. She was hospitalized because she became too weak to suck and swallow, and had a paroxysmal cough and, on the day of admission, 2 convulsions.

Physical examination showed an apathetic infant with cyanosis and great respiratory difficulty. Fine crepitant rales were heard throughout the chest, and x-ray study demonstrated widespread patchy infiltration of both lungs. The white-cell count was 45,000, with 60 per cent neutrophils. No cultures were made from the nose or throat.

On the ward she had a typical paroxysmal cough and generalized twitchings. She had to be fed for 11 days by gavage. After several paroxysms of coughing she was given artificial respiration, since spontaneous respiration seemed to have ceased. She was discharged on the 29th day apparently recovered.

She was not seen again until she was 14 years old, when she had just finished repeating the seventh grade in school. At that time she was overanxious — for example, she would not go to bed unless her mother went with her.

At 18 years of age she was an anxious, overweight girl. She had stopped school at the end of the tenth grade, when she was about to be 17. At that time psychologic examination was intellectually quite even, at about her age, giving an I.Q. of 95 to 100. Emotionally, she was dependent and immature. She still refused to go to bed alone. She would not leave the house alone and thought that people were watching her and talking about her. She was unable to hold a job consistently, and spent most of her time taking care of her aunt's children next door.

The final diagnosis was personality problem probably due to pertussis.

Since the occurrence of severe whooping cough complicated by pneumonia and encephalitis at ten weeks of age, this patient's development had been unequal, being average in the intellectual sphere but very retarded emotionally. Although she had been babied by her family, they had not, with fair insight, been able to avoid doing so.

Case 7. R. O. was the 1st child of healthy parents and was born normally at term. He did well for 4½ months and was definitely alert and responsive. Shortly before 4 months of age he visited some friends of the family where a child had a cold, later diagnosed as pertussis. A week later the patient had a cold and began to cough, lost his appetite and was fretful. About 2 weeks after the visit he began to whoop and vomit and lost considerable weight. Five days later he began to have generalized convulsions, increasing in frequency to 8 or 10 daily, and in severity from momentary to 3 or 4 minutes in duration. Four days before the convulsions began he received a dose of pertussis antigen, with doses repeated every 3rd day. After the third dose he was hospitalized.

On physical examination he was sluggish but otherwise not remarkable. The white-cell count was 20,000, with 73 per cent lymphocytes. The spinal fluid was clear, with no cells, a normal sugar and a total protein of 31 mg. per 100 cc.

In the hospital he had frequent paroxysms of coughing, with cyanosis and vomiting. He had numerous convulsions during the 1st week and became semicomatose. He required an oxygen tent for a week. He was discharged after 20 days, still with some cough and considerably less responsive than normal.

He was seen at 4 years and 8 months and at 6 years and 7 months. The convulsions did not recur. His physical development was slow but average, and neurologic examination was negative. Psychologically, he showed irregularities, with marked difficulty in form comprehension and a general mental level around 5 to 5½ years. He was unable to learn in the first grade, which he began at 6 years of age. Emotionally he was immature, dependent and suggestible. An electroencephalogram when he was last seen was definitely abnormal, with many scattered high-voltage spikes and runs of waves of 14 to 20 per second.

The final diagnosis was mental irregularity due to pertussis.

In this case, follow-up psychologic examination showed definite retardation, with irregularities strongly suggestive of brain damage. Emotionally the patient was also immature. An electroencephalogram strongly suggested the possibility of future convulsions.

Case 8. R. B. was born at term of healthy parents, by normal delivery, and did well in early infancy. She held her head up well at 4 months, and was sitting with support at 7 months. At 6½ months of age she was exposed to a visitor who had a cold, subsequently diagnosed as whooping cough. A week later a cough, which became paroxysmal, developed. At 7½ months of age she was admitted to the hospital with cough, vomiting and whoop. The white-cell count was 22,000, with 64 per cent lymphocytes. *H. pertussis* was grown from nasopharyngeal cultures. During the first 4 days in the hospital she vomited most of her feedings, and her weight declined from 14 pounds, 8 ounces, to 12 pounds, 12 ounces, although the paroxysms were not regarded as particularly severe. She had no symptoms suggesting acute involvement of the central nervous system. After this she gained satisfactorily and was discharged on the 12th hospital day.

Her development during the next several years was unsatisfactory as compared to that of her siblings. She walked at 14 months, did not use single words until after she was 3 years, was difficult to manage and at 3½ years was not yet toilet trained. Her mother refused several offers of psychometric examinations, but at 3½ years her behavior appeared more like that of a child 2 or 3 years old than of one 3 or 4 years old.

At the age of 5 years and 10 months she was seen by a psychologist, who found that, although she had an average intellectual level, her attention spans were short and her intellectual abilities variable. Visuomotor function and abstract reasoning ability were well below her age expectancy.

Her mother was also thought to be an immature, impulsive person, and it appeared that the child's mild irregularities might just as well be the result of inheritance and home environment as the result of brain injury incident to pertussis. Certainly, her functional level was more in keeping with her chronologic age at this time than it had been 2 years previously.

The final diagnosis was uncomplicated pertussis, with questionable temporary mental retardation due to the disease.

Case 9. J. M. was the 4th child of healthy parents of the professional class. The 2nd child had had natal and neonatal difficulties and was feebleminded, apparently because of a birth injury. The patient had a large angioma of the right side of the face involving the cheek, ear, and scalp up to the temporal ridge. This was treated repeatedly in the hospital with carbon dioxide snow, resulting in sloughing and cicatrization. Following this treatment, a cough developed at 4½ months of age. This became paroxysmal, with cyanosis, vomiting and whoop. On the 9th day the white-cell count was 46,000, with 84 per cent lymphocytes. On the 10th day the temperature rose to 103°F., and signs of consolidation appeared at the left base. She had 15 to 20 paroxysms of coughing daily for 2 days, when the temperature gradually declined and the cough subsided. She was discharged on the 23rd day, not having shown any neurologic symptoms.

Since the attack her physical development had been poor. At 17 years her height was 59 inches, and her weight 95 pounds, in a family all of whom were quite average in weight and height.

During infancy her development seemed quite comparable to that of the other children, as far as her mother was concerned. In school, however, she had difficulties with technical subjects, especially reading, and repeated the second grade, though she did not start school until she was 6½ years of age. At 17 years, however, she was doing well in the third year of high school and looking forward to college. On physical examination she showed no neurologic abnormalities.

The final diagnoses were hemangioma of the face, uncomplicated pertussis and questionable temporary mental irregularity due to pertussis.

On beginning school, this patient had unexpected difficulties with subjects depending principally on visual memory for success. As she advanced through school, her difficulties cleared up until, at seventeen years of age, she was well above average academically.

Her early school difficulties were of the type frequently resulting from mild diffuse cerebral injury, and her subsequent course could be explained either by a reversible encephalopathy, with recovery, or by the ability of a superior intellect to adjust itself to permanent damage or defect. The absence of neurologic signs made it appear unlikely that the hemangioma was intracranial as well as superficial.

Her variations from expectation were certainly minimal, but since they fitted a pattern shown by other cases, her case has been included as one in which whooping cough may well have produced marginal cerebral changes.

Case 10. A. G., the 2nd child of healthy parents, was born normally, and was alert and active. When he was 3½ months old the older sibling developed pertussis. At 4 months the patient developed a cough, which became paroxysmal, with cyanosis and vomiting. The temperature rose to 102°F., and since he was rigid and out of contact with his surroundings, he was hospitalized 2 weeks after the onset.

On physical examination he seemed stuporous but had no convulsions. He continued to eat fairly well. The white-cell count was 18,350, with 63 per cent neutrophils. A lumbar puncture showed a clear spinal fluid with no cells, a normal sugar, a total protein of 61 mg. per 100 cc., and no growth on culture. Two nasopharyngeal cultures showed no *H. pertussis*. His condition improved rather rapidly with return of temperature to normal on the 3rd hospital day, and his interest in his surroundings returned, though he continued to have paroxysms of whooping 6 to 8 times a day for several more days. He was discharged after 10 days in the hospital.

After discharge his development was slow. He began to walk at 2 years, and he began to use words at 3 years, but then speech developed rapidly. At 4 years and 7 months he appeared a happy adequate child, whose psychologic examination was entirely adequate, with no irregularities.

The final diagnosis was temporary mental retardation due to pertussis.

Discussion

Thirty-nine children who were admitted to the hospital with whooping cough, beginning between the ages of three weeks and twenty-three months, were followed. Three of them were already known to have had cerebral defects prior to their pertussis and were not further investigated. One child had measles with encephalopathy three months after the pertussis, and was also discarded from further consideration.

Of the remaining 35 children, 26 recovered apparently without residua; of these, 2 had encephalopathy on admission, and 4 more had cerebral symptoms while in the hospital.

Six children were found to have handicaps, permanently compromising their competitive status to a greater or lesser degree. Two certainly were feebleminded. Three have mental irregularities of the sort often accompanying diffuse cortical damage.[8, 9] Of these, 1 also had epilepsy. One more child, though showing average intellectual ability, was an emotional cripple.

Of these 6 children, 3 had obvious encephalopathy on admission to the hospital and in another one this complication developed in the hospital. In 2 cases, however, no suspicion of cerebral involvement was noted in the hospital.

Three children, 1 of whom had mild cerebral symptoms and a high spinal-fluid protein in the hospital, appeared to have suffered temporary developmental damage, from which recovery occurred after a period of years.

No cases of asthma or bronchiectasis were discovered in the children studied, though these conditions were sought by history and physical examination and in a few cases by plain x-ray films of the chest.

Conclusions

Since the present series was compiled from patients hospitalized for pertussis, and since 5 out of 35 were known to have encephalitis prior to admission and 8 pneumonia, the results were probably worse than those encountered in unselected cases of pertussis occurring during the first two years of life. Nevertheless, a finding of 6 noncompetent persons out of 35 cases seemed to us to indicate that pertussis early in life must be considered an important threat to competence.

Furthermore, though recovery to competitive level occurred after temporary developmental retardation, in 3 more cases it seemed entirely likely that these children's ultimate attainments had been somewhat compromised by the experience.

Many of the children studied were exposed to known cases of whooping cough, and could probably have been protected by the use of hyperimmune serum.

Finally, since pertussis vaccine seems prophylactically efficacious, the risks of its use in infancy[1] are probably outweighed by those of the disease itself.

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AMYLOID DISEASE WITH HYPERTENSION*

Report of a Case and Review of the Literature

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In the available literature there are only 39 reported cases of hypertension associated with amyloid disease. Classically, amyloid disease of the kidney is associated with a low or normal blood pressure.

In 1881 Dickinson[1] made the first reference to the occurrence of hypertension in amyloid disease. In 1894 Litten[2] reported 2 cases of hypertension with "Bright'sche Retinitis" occurring among several hundred cases of amyloid disease that he reviewed. Danisch,[3] Fahr,[4] Dixon,[5] Altnow, Van Winkle and Cohen,[6] Auerbach and Stemmerman[7] and Dahlin[8] have referred to single or several cases of amyloid disease with hypertension. However, these reports do not include pathological findings.

Table 1 summarizes the cases in the available literature in which the pathology of the amyloid kidney in cases associated with clinical hypertension is reported.

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Case Report

On August 18, 1942, a 21-year-old man was admitted to the hospital with a chief complaint of a draining sinus of the right knee of 6 years' duration and an intermittently draining sinus of the left hip of 3 years' duration. On November 18, 1935, he had been admitted to another hospital with a history of having struck his right knee previously, followed by local swelling and fever. The knee was incised and drained, and hemolytic *Staphylococcus aureus* was cultured. In subsequent years he had further drainage of the knee, and an abscess of the pelvis and buttocks had been incised and drained. In April, 1942, intravenous pyelograms showed no abnormality. At that time he had anemia and a palpable spleen.

The past history was otherwise noncontributory.

Physical examination revealed hepatomegaly and splenomegaly. Culture of the knee and hip sinuses grew out hemolytic *Staph. aureus*. Lipiodol injection of the sinuses revealed a tract extending as high as the second lumbar vertebra in the area of the left psoas muscle, with other droplets of Lipiodol overlying the sacrum, left sacroiliac joint and left os ischium. In addition, there was a deformity of the right femur at its distal end, with thickening of the epiphyseal portion. The knee joint was narrowed. There were coarse trabeculae at the metaphysis, with a cavity in this area. A sequestrum was thought to be present. The patient was given penicillin intravenously and locally. Although the cultures became bacteriologically negative, the discharge from the knee sinus recurred. He was discharged on January 31, 1943.

In April, 1943, he was readmitted on the Orthopedic Service for 5 weeks and given sulfadiazine, resulting in a

diminution in the quantity of discharge from the knee sinuses. In September he was again treated with penicillin intravenously and was discharged 3 months later, when he was afebrile and considerably improved although the sinuses were still draining.

On November 8, 1945, he was again readmitted to the hospital because of an acute exacerbation of the sinus of the left hip with a left-sided pelvic abscess. In addition to penicillin, incision and draining of the left pelvic abscess and excision of the sinus tract and scar tissue at the distal end of the right femur were performed. At the time of discharge on May 3, the right femur was still draining, and hemolytic *Staph. aureus* was still cultured. During this admission the average blood pressure was 130/80.

The next admission was on March 3, 1947, on the Surgical Service, where a blood pressure of 194/132 was noted for the first time. On transfer to the Medical Service, physical examination revealed cardiac enlargement and early hypertensive eyeground changes. The sinus of the right knee was draining, with marked limitation of motion of the joint. A phenolsulfonphthalein test showed 3 per cent excretion of the dye in 15 minutes and 18 per cent total excretion in 2 hours. The white-cell count was 11,000. The hemoglobin, which early in the course had been low, was 14.5 gm. per 100 cc. The sedimentation rate was 55 mm. per hour. X-ray examination showed a decrease in the size of the kidneys and considerable enlargement of the spleen. Hypertrophy and dilatation of the left ventricle were also confirmed by x-ray study. On April 18 a sequestrectomy of the right femur was performed. Postoperatively, he received 2 gm. of streptomycin daily for 10 days. On the 14th postoperative day, the sinus tract ceased to drain for the third time in 12 years. On transfer to the Medical Service on May 13, the blood pressure was 160/110. Retinal exudates, blurring of the disk margins and arteriovenous nicking were noted. The blood pressure, after the patient had been placed on a salt-free rice diet, varied from 175/130 to 150/70, and the nonprotein nitrogen dropped to 35 mg. per 100 cc. Kidney-function studies* revealed a mannitol clearance of 19.5 cc. per minute per square meter and para-aminohippuric acid clearance of 95 cc. The maximum tubular excretion of para-aminohippuric acid was 15 mg. per minute per square meter. At discharge he was placed on a low-protein, low-salt diet.

The patient was readmitted to the hospital for evaluation of his hypertension on January 13, 1948. He had had no further drainage from the osteomyelitic sinuses since the previous May. He had had no dyspnea and only rarely had headaches. The blood pressure on admission was 180/130. The hematocrit was 32 per cent, and the hemoglobin 11 gm. per 100 cc. The patient was discharged after 3 days when Vertavis (veratrum viride) dosage had been regulated so that occasional blood-pressure readings were as low as 115/60.

Two weeks prior to readmission on March 4, 1948, the patient had an attack of epistaxis, and thereafter had them almost daily, lasting as long as 4 hours. He had also noted, for the 10 days prior to readmission, cramping in the legs severe enough to awaken him. Because of a severe anemia

*Renal-clearance studies were performed by and are included by permission of Dr. Charles Burnett, Robert Dawson Evans Memorial, Massachusetts Memorial Hospitals.

TABLE 1. *Cases in the Literature with Reports of Pathologic Kidneys.*

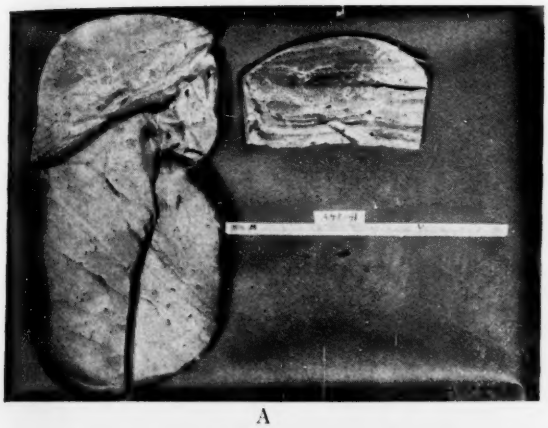
AUTHOR	AGE	SEX	BLOOD PRESSURE	PRIMARY DISEASE	KIDNEY DISEASE
	yr.				
Noble and Major[9]	35	F	176/104	Osteomyelitis of left tibia for 11 yr.	Nothing on gross examination to suggest amyloid
Fishberg and Oppenheimer[10]	37	M	196/116	Tuberculosis of left hip for 32 yr.	Amyloid, contracted kidneys
Bell[11]	50	F	170/120	Syphilis	All patients had massive deposits of amyloid in glomeruli, with slight or marked tubular atrophy
	46	M	238/142	Empyema for 12 yr.	
	35	F	190/110	Primary amyloid disease	
Sackey[12]	41	M	190/120	Tuberculosis, with massive fibrosis of lung	Amyloid, contracted kidneys
Perla and Gross[13]	18	F	180/94	Atypical primary amyloidosis	Amyloid, contracted kidneys; each weighed 50 gm.
Gerber[14]	44	M	—	Primary amyloidosis	Right kidney weighed 120 gm.; left kidney weighed 110 gm.
Mark and Mosenthal[15]	42	F	190/98	Pulmonary tuberculosis for 14 yr.	Combined weight of kidneys was 280 gm.

TABLE 2. *Clinical Course.*

DATE	AGE	SIZE OF LIVER	SIZE OF SPLEEN	CONGO-RED RETENTION	BLOOD PRESSURE	URINE		NON-PROTEIN NITROGEN	TOTAL PROTEIN	WEIGHT
						SPECIFIC GRAVITY	ALBUMIN			
	yr.			*%*				*mg. per 100 cc.*	*gm. per 100 cc.*	*lb.*
8/42	21	Palpable 2½ finger-breadths below costal margin	Palpable	100.0	120/58	1.022	0-++	29	6.7	132
9/43	22	Palpable 6 cm. below costal margin	Palpable 3 cm. below costal margin	57.6	108/68	1.014	+-+++	55 27	4.8 6.78	136
11/45	24	Palpable 4 cm. below costal margin	Palpable	32.0	130/80	1.016	(17.9 gm. in 24 hr.)	56	7.06	193
4/47	26	Palpable 4 cm. below costal margin	Palpable at costal margin	—	170/125	1.010 (fixed	++-++++	67 38	5.15	192
1/48	26	Not palpable	Not palpable	—	180/130	1.010	++++	—	—	166
3/48	27	Palpable at costal margin	Percussible	—	160/100	1.010	++-+++	183 216 157 178	5.39	166

he was readmitted to the hospital. The sedimentation rate was 12 mm. per hour, the hematocrit 22 per cent, the hemoglobin 7.2 to 8.5 gm. per 100 cc., and the platelet count 320,000. The bleeding time was 18 minutes, the clotting time 8 minutes, and the prothrombin time 39 per cent of normal. The white-cell count was 6500. The carbon dioxide content was 11.6 milliequiv. per liter, which rose to 29.5 milliequiv. Table 2 lists other details of the clinical course.

The patient was given 10 per cent glucose in 50 per cent physiologic saline solution and 50 per cent one-sixth molar sodium lactate. He continued to vomit and was unable to eat. Despite further intensive therapy, he became stuporous on March 10 and died 10 hours later. The final clinical



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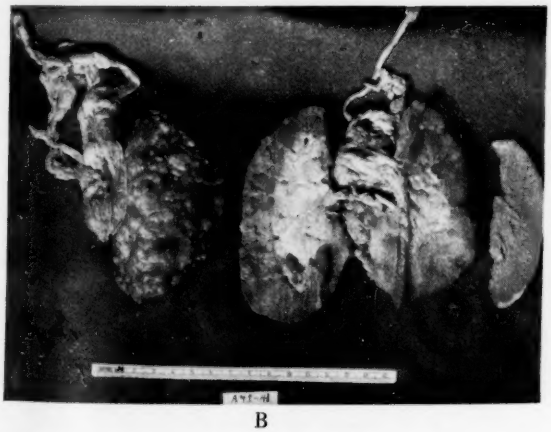

B

FIGURE 1. *Gross Appearance of the Liver and Kidney.* A = *liver, showing circumscribed deposition of amyloid, which merges sharply with the surrounding liver parenchyma.* B = *kidneys, showing nodularity of external surfaces and indistinct corticomedullary demarcation.*

diagnoses were amyloidosis of the kidney, liver and spleen; hypertension, secondary to amyloid disease; heart disease, hypertensive; uremia; chronic osteomyelitis of the right knee and left ilium, healed; and terminal bronchopneumonia.

Post-mortem examination showed numerous scars of previous sinus tracts and operative procedures. The right patella was fused to the anterior aspect of the tibia, and motion of the knee joint was limited to approximately 25°. The liver extended 13 cm. below the xiphoid, 6 cm. below the right costal margin in the anterior axillary line and 5.5 cm. below the left costal margin in the left midclavicular line. It was smooth externally and very firm posteriorly, containing a circumscribed deposition of amyloid that merged sharply with the surrounding parenchyma (Fig. 1*A*). The spleen was enlarged. The kidneys were reduced in size. Numerous discrete, rubbery lymph nodes were noted in the root of the mesentery. On cut section they were waxy and salmon pink. The pericardial cavity contained 50 cc. of clear, serous fluid.

The heart weighed 420 gm., the lungs 1400 gm., the spleen 460 gm., the liver 2180 gm., the pancreas 120 gm., and the adrenal glands 40 gm. The lungs revealed diffuse acute pulmonary edema and patchy acute bronchopneumonia. The liver showed evidence of amyloidosis on cut surface. The gall bladder contained two pigment calculi, which were lodged in the ampulla.

The right kidney weighed 110 gm., and the left 120 gm. The kidneys were small but assumed a normal shape and position. The capsules were pinkish gray and stripped with a slight amount of difficulty. The external surfaces were brownish red and roughly lobulated. These lobules were yellow, varying in size from 0.1 to 1.6 by 1 by 0.3 cm., and were irregular in shape, often appearing as conglomerate lobules. Cut surface revealed poor corticomedullary demarcation (Fig. 1*B*), with cortices varying up to 0.3 cm. in width and completely absent at the poles. The pyramids could still be made out with ease but were somewhat obliterated by the orange cast. The cut surfaces were much firmer in consistence than usually noted and when placed in Lugol's solution took on a mahogany-brown color.

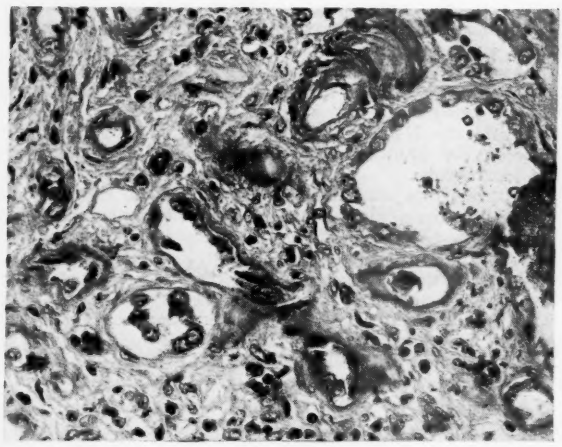

FIGURE 2. *Photomicrograph of the Kidney, Showing Complete Occlusion of Prearterioles by Amyloid Deposition, Amyloid Surrounding Tubules and Compensatory Hypertrophy of Tubules (Phloxine Methylene Blue Stain x 400).*

There was no evidence of active infection in the pelvis or knee area. The other organs and vessels were normal on gross examination.

For microscopical examination all sections were fixed in Zenker's fluid and stained routinely with phloxine-methylene-blue. Sections were stained for amyloid with cresyl violet and Congo red.

The heart revealed hypertrophy of the cardiac muscle and coronary arteriosclerosis. The lungs revealed an acute bronchopneumonia and acute pulmonary edema, with acute and chronic bronchitis. In an occasional area there were fibroblasts ingrowing from alveolar walls. The hilar lymph nodes showed acute lymphadenitis and amyloidosis.

Sections of the spleen and accessory spleen revealed amyloidosis and focal acute congestion and hemorrhage. The trabecular arteries and arterioles of the pulp were practically all the seat of amyloid deposition. The lumens were narrowed or obliterated. There were occasional areas of amyloid between the cells of the white pulp, and in the reticulum of the red pulp in a few places.

The liver showed a moderately advanced amyloidosis. The extent varied from involvement of small portions to complete replacement of the liver lobules. Some cells showed pressure atrophy and degeneration. Where the condition was advanced there was frequently persistence of Kupffer cells and the spaces representing the sinusoids. The periportal

structures were preserved in most areas, and there was always a narrow, free subcapsular zone. The hepatic arterioles frequently displayed amyloidosis.

The arteries and arterioles of the gall bladder and especially the mucosal regions demonstrated amyloid deposition in their walls. The lumens of the pancreatic arteries and arterioles and peripancreatic fat vessels were narrowed to obliterated by amyloid deposition. Not infrequently, only a segment of the circumference of the arteriole was involved.

The mucosa of the stomach and small intestine revealed amyloidosis. The arterioles and capillaries of the lamina propria showed marked narrowing to obliteration with amyloid deposition.

The kidneys displayed a marked amyloidosis involving glomeruli, tubules and arterioles (Fig. 2). Practically all the glomeruli were affected in various degrees. Frequently, the tubules of uninvolved glomeruli were dilated, hypertrophic and filled with albuminous precipitate. In other areas they were atrophic and displayed degeneration necrosis. The prearterioles and afferent arterioles displayed amyloidosis, with varying degrees of lumen obliteration. The intertubular arterioles were also involved.

The adrenal glands showed a marked degree of amyloidosis. The amyloid appeared to be deposited between the endothelial cells and cortical cells of the zona fasciculata and reticularis. In some areas cortical cells were absent. The zona glomerulosa did not appear to be involved, and the medulla was only slightly involved.

There was a narrow zone of slight amyloidosis in the lamina propria of the urinary bladder. The seminal vesicle in one section showed marked amyloidosis. The pars anterior of the pituitary gland revealed a patchy amyloid deposition between the sinusoids and cells. The brain sections were not remarkable.

Culture of the heart, blood and spleen disclosed no growth.

The anatomic diagnoses were healed osteomyelitis, with fusion of the right patella to the right tibia; amyloidosis of kidneys, liver, adrenal glands, lymph nodes, spleen, gall bladder, pancreas, stomach, small intestine, urinary bladder and hypophysis; cardiac enlargement; hypertrophy of the right and left ventricles and dilatation of the right auricle; pleural adhesions, fibrous; hydropericardium, slight; and chronic cholecystitis and cholelithiasis.

Discussion

This case confirms pathologically the usual finding of contracted kidneys in amyloid cases with hypertension previously reported in the literature (Table 1). Contracted kidneys are also found in cases of amyloid disease without hypertension. Fahr's[4] cases of hypertension in amyloid disease were in young people who were well nourished, whereas in his patients with cachexia, blood pressures were low. The patient discussed above was very well nourished, weighing 166 pounds on his final admission before edema became evident. It therefore appears that body nourishment in amyloidosis may be a factor in determining blood pressure in this group of patients.

Pathologically, besides marked amyloid deposition in all parts of the kidney, depositions of amyloid were noted in the arterioles and smaller vessels of the spleen, liver, gall bladder, lamina propria of the stomach, prearterioles and afferent arterioles of the kidney, pancreas and periadrenal fat. The narrowing of these vessels is usually noted in advanced essential hypertension, but in this case the substance responsible was amyloid instead of the usual hyaline deposition.

It should be noted that this is the second youngest patient with hypertension and amyloid disease that could be found in the available literature.

It is also of interest that the osteomyelitic process had become inactive after nitrogen retention developed.

Summary

A case, with autopsy findings, of hypertension secondary to amyloid contracted kidneys and visceral arteriolar amyloid deposition occurring as a result of chronic osteomyelitis is reported. A review of hypertension associated with amyloidosis is presented.

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CARCINOMA OF THE CERVIX

A Report of 200 Cases Treated with Radium and X-Rays

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NEARLY ten years ago a previous paper† covered a review of 200 consecutive cases of carcinoma of the cervix treated with radium from 1920 to 1934; 185 of these cases were primary carcinomas, and 15 were carcinomas of the cervical stump. The five-year survival without evidence of disease in the 185 primary cases was 70 patients, or 37 per cent. All patients were treated with radium, with approximately the same dosage and the same method.

In that paper the wish was expressed "that a further report may be presented later, in which these results will be compared with those in a series in which the same radium technic will be supplemented by preliminary deep x-ray therapy."

Herewith is presented a second series of 200 consecutive primary carcinomas of the cervix treated from 1934 to 1944, all treated with the same method as the first group and by the same two surgeons. The only difference in treatment was the addition of x-ray therapy prior to radium therapy. Most of the x-ray treatments were given by Dr. A. S. Merrill at the Elliot Hospital, but some were given at two other clinic treatment centers. The total x-ray dosage varied from 7600 to 9000 r.

The anticipated improvement in final results of this second series did not fulfill the hopes previously expressed: the five-year survival without evidence of disease in the second series of 200 cases was 74, or 37 per cent — exactly the same as the results in the treatment of 185 patients with radium alone.

Table 1 compares the results in the two series, including the number and percentages of patients in each stage according to the League of Nations classification. In the first series the total of five-year survivals was 70, or 37 per cent, as compared with 74, or 37 per cent, in the second.

It is to be noted that Stage I cases in the second series showed a higher (67.2 per cent) five-year salvage than in the first series.

Table 2 reveals a larger number of patients in Stages I and II in the second series. This is believed to be due to the continued and widespread educational campaign against cancer carried on in New Hampshire since 1936.

It is impossible to explain why, in the first series treated with radium alone, patients in both Stage II and Stage III showed a higher percentage of five-year survivals than those in the second series given the same radium treatment and adequate x-ray therapy. Consideration must be given, of course, to probable errors in the clinical estimation of Stages II and III. The differentiation between these two stages is often difficult, especially when there is some inflammatory reaction. Each of the 385 patients was classified for the clinical stage, however, by one and sometimes by two surgeons, as accurately as possible.

The basic principles of the radium technic have been carried out as outlined below except for minor changes required because of location of growth and amount of reaction to treatment. Each patient was given 0.03. gm. (1/2 gr.) of Pantopon and 0.2 gm. (3 gr.) of Nembutal one hour before the treatment, and no general anesthesia was used unless the patient was very unco-operative. The cervical

TABLE 1. *Comparative Results in Two Series of Cases.*

STAGE	SERIES OF 1920-1934*				SERIES OF 1934-1944†			
	TOTAL PATIENTS	PER-CENTAGE	NO. OF SURVIVALS	PER-CENTAGE	TOTAL PATIENTS	PER-CENTAGE	NO. OF SURVIVALS	PER-CENTAGE
I	38	29	24	63	58	2..0	39	67.2
II	21	11	11	52	58	29.0	21	36.2
III	98	53	35	35	63	31.5	14	22.2
IV	28	15	0	—	21	10.5	0	—

*185 patients, of whom the oldest was 84 and the youngest 26 yr. of age (average age, 49 yr.).
†200 patients, of whom the oldest was 81 and the youngest 28 yr. of age (average age, 49.7 yr.).

TABLE 2. *Stage in Which Patients with Carcinoma of the Cervix Apply for Treatment.*

STAGE	PATIENTS IN 1920-1934	PATIENTS IN 1934-1944
I-II	32	58
III-IV	68	42

*Surgeon emeritus and director of Cancer Clinic, Elliot Hospital.

†Wilkins, G. C. Carcinoma of cervix: review of 200 cases treated with radium. *New Eng. J. Med.* **224**:414, 1941.

canal was slowly and carefully dilated with Hanks dilators. With 100 mg. of radium in two brass screens (2.0-mm. wall), 75 mg. was placed in the cervical canal and 25 mg. just above, for twenty hours. On the second day after this, another treatment was given with the same amount of radium in a T tube, with 50 mg. in the canal and 50 mg. in the crosspiece, the crosspiece being either anteroposterior or transverse, as indicated by the location of the lesion. This applicator remained for eighteen hours. With all treatments, the vagina was firmly packed with gauze, and an inlying catheter placed in the bladder. Three weeks later, the third and last treatment was given, usually a repetition of the first, for eighteen or twenty hours. These three treatments totaled 5600 to 5800 milligram hours.

It is believed that the spacing of treatments is important. It was found that the first two treatments given within forty-eight hours of each other, and totaling 3800 milligram hours, were about all a patient could have without producing too intense bladder or rectal irritation. It was also found that in three weeks practically all radium reaction had subsided; this was considered the best time for a third treatment — one that would deliver another blow to any cancer cells that had not received a lethal dose.

The importance of this timing, which was decided upon empirically, was subsequently found to approximate closely the theory of Coutard regarding the periodicity of susceptibility of cancer cells to irradiation.

In the treatment of the latest 200 patients, radium therapy was instituted three weeks after the end of x-ray.

The preliminary x-ray therapy was found to have several advantages. Bleeding usually ceased shortly, vaginal discharge decreased, inflammatory reaction subsided and by the time the patient was ready for the first radium treatment, most or all of the cauliflower type of growth had disappeared and the invasive ulcerative growths were smaller. These changes made for easier and more accurate radium applications.

Five patients were given only two radium treatments — in 2 because further therapy was deemed inexpedient. One Stage I patient died of peritonitis four weeks after two radium treatments. Her physician's diagnosis had been pelvic inflammation, probably of gonorrheal origin. A patient in Stage III died two weeks after the second radium treatment. Her physician's diagnosis had been intestinal obstruction. And 1 Stage II patient, who had auricular fibrillation when admitted for treatment, died at home five days after the second treatment of myocardial failure.

Vesicovaginal fistula due to treatment and not to advancing terminal disease developed in only 1 patient. She was well ten years after treatment.

Pathological diagnoses of squamous-cell carcinoma of various grades were made in 192 cases, highly malignant carcinoma in 4, carcinoma in 2, adenocarcinoma in 1, and adenoacanthoma in 1.

Summary

A series of 185 previously reported cases of primary carcinoma of the cervix is reviewed, and a new series of 200 cases reported.

The first series of 185 patients treated with radium alone showed a five-year salvage without evidence of disease of 70 patients, or 37 per cent. The second series of 200 patients given preliminary x-ray therapy and with the same radium technic showed a five-year salvage without evidence of disease of 74 patients, or 37 per cent.

All radium treatments given the 385 patients were by me or an associate. Although definite clinical advantages were observed to result from the preliminary x-ray therapy, the final results obtained in the two series indicate the comparative ineffectiveness of x-ray therapy in influencing the curability of carcinoma of the cervix and reaffirm the position that adequate radium therapy is the important agent in radiation therapy of the cervix.

DILANTIN SENSITIVITY*

Report of a Case of Hepatitis with Jaundice, Pyrexia and Exfoliative Dermatitis

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THE use of Dilantin Sodium (sodium diphenyl hydantoinate) has become widespread since the introductory study by Merritt and Putnam,[1] who described certain toxic effects in the course of its administration. These are chiefly referable to the central nervous system, gastrointestinal tract, skin, gums and hematopoietic system. They observed cutaneous lesions in 5 per cent of their cases. These varied from mild erythema to a diffuse morbilliform eruption and, in 1 case, severe generalized exfoliative dermatitis. The incidence of the toxic effects of Dilantin have varied from 58 per cent [2] to 93 per cent [3] in a number of subsequent reports.[2-12] Fortunately, the majority of these are mild, and do not constitute contraindications to the use of the drug. As has been repeatedly stressed, patients receiving this drug should be under periodic and prolonged observation since severe systemic reactions[8, 10, 12] and even death may ensue.[8, 9, 13]

The case presented below is of interest because of the occurrence of hepatitis with jaundice, eosinophilia, exfoliative dermatitis, generalized tender lymphadenopathy, pyrexia, prostration and severe localized muscle tenderness. The nature of this clinical picture remained obscure until, when the administration of Dilantin was resumed, an exacerbation of these clinical findings occurred. We believe this to be the first reported case of hepatitis with jaundice due to Dilantin sensitivity.

CASE REPORT

J. J., a 29-year-old Negro who was known to have had epilepsy since early childhood, had never been on specific therapy until August 14, 1949, when he first reported to the Neurology Clinic of the Boston City Hospital. At this time, he was given Dilantin Sodium, 100 mg. three times a day. After consuming 49 capsules (4.9 gm.) over a period of approximately 17 days, he noted the development of malaise, anorexia, nausea and generalized muscle aches. He thereupon ceased taking the medication at that time, 3 weeks prior to admission. These symptoms persisted, however, and 1 week before admission a generalized pruritic rash and yellowing of the scleras, which was first observed by his wife, developed. This was accompanied by shaking chills and a maximum daily temperature of 105°F. Generalized abdominal pain, described as aching, was experienced, at times becoming severe and lancinating, although without specific localization. This pain was accompanied by vomiting. There was generalized muscle tenderness, and large tender lymph nodes in the cervical, axillary and inguinal regions were noted. The urine was described as "brownish."

The patient denied having received recent transfusions or injections of any sort. There was no known contact with any jaundiced patients or persons with any serious illness, and he denied ingestion of unpasteurized milk or water of unusual source. Although he had detected the presence of rats in the warehouse where he worked, he had never been bitten. He had never had malaria, and denied syphilis by name and symptoms. He had never been in tropical regions, his entire life having been spent in South Carolina, Michigan and Massachusetts. No contact with noxious chemicals occurred in his occupation. The patient denied alcoholic intake.

There was no history of asthma, hay fever or other allergy in the past, and no known epilepsy, allergy or other diseases of contributing importance in the family history.

Physical examination showed a patient who appeared acutely ill, was markedly prostrated and manifested signs of dehydration. The skin was dry, with poor turgor, and presented a diffuse morbilliform rash involving the face, body and extremities, accompanied by severe pruritus. No subcutaneous nodules were felt. The scleras were icteric, and the conjunctivas were injected. There was a moderate degree of facial and periorbital edema. The pharynx was slightly injected, with tonsils of normal size and several small, pink spots over the palate. The gums were hyperemic and showed early evidence of hypertrophy. The neck was supple, and the cervical lymph nodes were enlarged and exquisitely tender. The lung findings were entirely negative as were the cardiac, except for a pulse rate of 100. Examination of the abdomen revealed a generalized "soreness" on palpation, most marked in the right upper quadrant and epigastrium, but there was no localized spasm. The liver was palpable and extended three fingerbreadths below the right costal margin; the superior margin was percussed at the level of the fifth right interspace. Its margin was smooth, and a good deal of tenderness was elicited on palpation of this organ. The spleen was not palpable. Enlarged axillary, epitrochlear and inguinal lymph nodes were present and extremely tender. Both lower extremities revealed excessive muscle tenderness on compression. Rectal examination was negative. The central nervous system showed no objective abnormal findings.

The temperature was 105°F., the pulse 100, and the respirations 20. The blood pressure was 110/68.

Examination of the blood disclosed a white-cell count of 8000, with 27 per cent neutrophils, 43 per cent normal and 24 per cent atypical lymphocytes (the atypical lymphocytes were large, with eccentric, lobulated nuclei and foamy cytoplasm) and 6 per cent eosinophils. The sedimentation rate was 8 mm. in 1 hour, the icteric index 37, the hemoglobin 14.5 gm. per 100 cc., and the reticulocyte count 1.5 per cent. Sickling could not be demonstrated by the sodium bisulfite test, and no malarial parasites were found on thick smear examination. The urine revealed the presence of bile, and urobilinogen in a dilution of 1:160. No sugar, albumin or acetone was found, and the sediment was normal. The stools were not acholic, and tests for occult blood, ova, amebas and parasites were negative.

Pyrexia continued, remittent in type, with daily temperature rises to 105°F. The patient appeared very toxic, and in a critical state. Fluids were administered parenterally, and he was given trial periods of penicillin and Chloromycetin therapy, without influence on either the course of his clinical condition or the pyrexia. The rash, which had originally been morbilliform, became vesicular and then began to desquamate. X-ray films of the chest and abdomen taken in the interim revealed no abnormalities of the heart or lungs, and the shadow of the liver was visible down to the level of the third lumbar vertebra.

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On the 4th hospital day the white-cell count was 16,400, with a rise from the initial eosinophil count of 6 to 20 per cent. The atypical lymphocytes, previously described, were 6 per cent at this time. The leukocytosis and eosinophilia persisted; on the 8th day the white-cell count was 23,550, with 22 per cent eosinophils. With the rise in eosinophils there was a gradual disappearance of the atypical lymphocytes. Serial examinations at weekly intervals for heterophil antibodies were negative. The blood Hinton test was negative. The icteric index rose to 50 but at the end of a week showed gradual subsidence. The cephalin-cholesterol test was ++ in 48 hours, remaining at that level until the 3rd week, when it dropped to +, and finally became negative after 4 weeks. At the end of 3 weeks, when the icteric index had dropped to 10, the bromsulfalein test revealed 4 per cent retention of the dye in 45 minutes. The urine was clear of bile after 1 week and urobilinogen showed successive tests of 1:160, 1:60, 1:40 and 1:20 in the course of 2 weeks. Urine cultures were all negative, as were repeated blood cultures utilizing aerobic and anaerobic mediums. Search for Leptospira by means of dark-field examination proved fruitless; their absence was confirmed by guinea-pig inoculation and negative agglutination tests for *Leptospira icterohaemorrhagicae* and *canicola*.* Nasopharyngeal cultures revealed alpha-hemolytic streptococci, *Neisseria sicca*, *N. flava* and diphtheroids. Stool cultures were negative. Lumbar puncture demonstrated a normal spinal-fluid pressure with a negative Pandy reaction and a protein content of 36 mg. per 100 cc. There were no cells, and culture showed no growth. An electrocardiogram on the 2nd day was normal.

Agglutination tests for typhoid, paratyphoid, brucella and tularemia were negative, as was the Weil–Felix test. Skin tests for trichinosis showed negative reactions. A blood bromide level was reported as too low to be recorded.

Bone-marrow aspirations revealed 21 per cent eosinophils and 9 per cent eosinophilic myelocytes on the 8th day, 57 per cent eosinophils on the 10th day and 15 per cent eosinophilic myelocytes on the 26th day. (The eosinophilic cells showed no abnormal morphologic characteristics.) Biopsy of an enlarged cervical lymph node and a segment of the gastrocnemius muscle was performed on the 12th day. The examination of a lymph node disclosed "chronic inflammation," and no arterial or other lesions were manifest in the muscle. At the time of the muscle biopsy, most of the muscle tenderness had subsided.

Despite the numerous studies, a definite diagnosis was not apparent. However, the patient continued to improve clinically on a high-protein, high-carbohydrate diet with supplementary vitamins. The rash cleared, the fever disappeared after 2 weeks, the lymph nodes diminished in size, and the liver edge receded. Five weeks after admission his convalescence was progressing satisfactorily.

Possible relation to the Dilantin taken by the patient was not considered, because of the severity of his illness, which at one time was critical, and the fact that reports of reactions to Dilantin of this severity had not come to our attention.

Therefore, when, during the 5th week, the patient had a typical grand-mal convulsion he was again given doses of 100 mg. of Dilantin. After the third dose he began to complain of malaise, and the morbilliform pruritic eruption reappeared. The eosinophils, which had previously disappeared, promptly rose to 10 per cent. There was no enlargement of the liver, and the cephalin-cholesterol test remained negative. With immediate cessation of the drug, the symptoms regressed, and the eruption disappeared.

Discussion

In the case presented above, marked remittent pyrexia, abdominal pain, muscle tenderness and prostration were accompanied by hepatomegaly, jaundice, lymphadenopathy, eosinophilia and a morbilliform eruption that progressed to a true exfoliative dermatitis.

Jaundice may occur after the administration of several types of drugs. The damage to the liver from chloroform and carbon tetrachloride is undoubtedly a direct toxic effect. In the reactions to sulfonamides, cinchophen, quinacrine hydrochloride and arsphenamine, there is reason to believe that jaundice results from a true hepatitis caused by sensitivity.[14, 15]

A search of the literature indicated the similarity of this case to several due to severe Dilantin sensitivity. Mandelbaum and Kane[12] reported a case of exfoliative dermatitis and pyrexia, with hepatic and splenic enlargement, due to Dilantin sensitivity followed by recovery. Van Wyk and Hoffmann[13] described a case of severe systemic reaction, exfoliative dermatitis, eosinophilia and death following Dilantin therapy in which autopsy revealed hepatic enlargement with fatty degeneration of the liver and lesions of periarteritis nodosa. Neither patient manifested jaundice. The sulfonamides,[16, 17] as well as other drugs,[13, 15] have been incriminated in the etiology of many of these reactions.

Muscle biopsy in the case reported above, taken after muscle tenderness had subsided, was perhaps tardy and yielded negative results.

Summary

A case of severe Dilantin Sodium poisoning, which appears to have been a true drug-sensitivity reaction, is reported. This is believed to be the first report of the occurrence of hepatitis with jaundice due to Dilantin. This case serves as a reminder of the necessity for continued close surveillance of all patients receiving the drug.

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MEDICAL PROGRESS

RECOGNITION, TREATMENT AND CONTROL OF POLIOMYELITIS*

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THOUGH poliomyelitis has been held by some to have existed as early as 1600 B.C., the first careful clinical description of the malady was given by Underwood[1] in 1789. Bell,[2] in 1836, described the case of a child "who had one leg much wasted in growth," as a result of an epidemic among the young children of St. Helena. He observed that these children had "a want of growth in some part of their body or limbs" and concluded, "This deserves to be inquired into."[3] Scientists in many related fields of research have been investigating every conceivable point of approach to the solution of the many-faceted "unknowns" of poliomyelitis, particularly its mode of transmission and its prevention and treatment.

About a century and a half ago (1843) poliomyelitis made its appearance in this country, attacking a few infants under two years of age in Louisiana, followed in 1894 by an epidemic of 132 cases in Vermont.[4] No epidemic occurred in any part of the world before about 1870.[5] Curiously enough, in the past sixty years, when other infectious diseases have been declining, poliomyelitis has appeared with increasing frequency in this country.[6] Its appearance in any community, rural or urban, is heralded by alarm of varying magnitude, approaching in some instances terror[5, 7] and "neurotic behaviour."[8] Heavy is the responsibility resting on the physician not only in his own sphere of healing but also in the larger sphere of public relations, that recent advances in knowledge of poliomyelitis may be disseminated and undue anxiety allayed. With poliomyelitis occupying the spotlight of a prodigious amount of research, there have been marked changes in opinion and additions to concepts previously held. Of necessity, many present theories related to poliomyelitis, though formed from precise observations of many scientists, cannot be proved as yet, and may never be crystallized. But enough of the "new" has transpired to impress one with the decided advance in understanding poliomyelitis as compared with theories of only a score of years ago. What, then, are current concepts of the disease?

CONCEPT OF ETIOLOGY

Poliomyelitis is a disease of world-wide[9] distribution caused by a virus with a special affinity for nervous tissue. Greater insight into the complex problem of management of poliomyelitis results when one considers the possible portals of entry into the body and probable behavior of the virus after entry is made.

There are three possible portals of entry: the skin, the oropharynx and the alimentary tract.

At the turn of the century infantile paralysis was classically described as a disease rare after six years of age.[10] This is no longer true.[11] The shift in age distribution of poliomyelitis has been widely noted by many authors.[5, 12-16] Horton[16] attributes it to a "greater dispersion of population in rural areas" causing fewer cases early in life and consequently more in the older age group. Automobile travel and consolidation of rural schools increases probability of contact and thus induces an earlier acquired immunity. In such countries as Chile[13] the Dominican Republic,[13] Guatemala,[13] Iraq[13] and the Far East[9] poliomyelitis is still endemic, occurs in the younger age group and is often of the "spinal form."[13]

By contrast, in the United States, Sweden, Denmark,[9] France,[13] Great Britain,[9] New Zealand,[13] Australia,[17] Switzerland[13] and countries of comparable sanitary standards, poliomyelitis has changed from endemic nature to epidemic, with older age groups now affected. At present it is generally agreed that more people reach adolescence and adulthood without becoming immune because standards of sanitation prevent subclinical infection in childhood.[7, 15, 17, 18] Jungeblut[14] noted that in guinea pigs advanced age "enhanced the resistance to paralytic involvement," which he states cannot be explained by specific immunologic influences. In World War II, when United States and British troops were stationed in such areas as Japan and the Philippine Islands, where sporadic cases occur among the native population in the age group under two years, military personnel contracted poliomyelitis in some cases at a rate ten times that of the native population.[6, 7, 18] Since the virus was widely prevalent, the native population had acquired an immunity not enjoyed by the vulnerable military personnel.[6] Strains of poliomyelitis virus may also have differed in this locale, presenting the possibility of a "strain-specific immunity."[6] In a study of 149 fatal cases in United States Army hospitals during 1944-45, the incidence of the disease was lower as compared with that in the general population, though the mortality was higher in the military age group.[19]

*The Prize Essay for 1950.

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Poliomyelitis is no respecter of class or economic status, since it probably occurs more often in the well nourished.[18, 19] There has been no change in previous data indicating that poliomyelitis attacks the male more frequently, shows no predilection for race, but occurs two to three times more often in rural than in urban centers.[1] Likewise, the incidence continues to parallel the onset of warm weather, occurring earlier in southern states than in northern ones.[5] The peak of the outbreak is usually during the month of August.[13] Molner[1] has advanced a novel explanation for the higher incidence of poliomyelitis occurring in the temperate zones. He suggests that a greater number of people do not make "adequate physiologic adjustment" with the changes in climate, making them more susceptible to disease.[1] According to Aycock,[20] exposure to poliomyelitis, as to diphtheria and scarlet fever, occurs at an earlier age in warmer climates, is probably more extensive and thus results more frequently in a modified infection, with consequent active immunity. Howe[4] epitomizes the newer concept of age selection in poliomyelitis as the "acquisition of specific immunity."

Mode of Transmission

Satisfactory solution of the mode of transmission would simplify management and control of the disease. In recent years, there have been advances in this direction. Various means of transferral of virus to human beings have been suggested, such as transmission by an arthropod vector with or without an intermediate reservoir, contamination of food or water on a large scale, contamination of hands or playthings by feces or pharyngeal secretions, and droplet infection.

Search continues for a reservoir, one of the latest possible carriers of the virus to be considered being the ground mole.[21, 22] A point in favor of spread by insect vector is the nature of the poliomyelitis outbreak: seasonal, localized and with sudden rise and fall in the number of patients.[5] On the other hand, evidence is lacking that the disease is propagated by a blood-sucking insect[17, 23] — to date there have been very few reports of isolation of virus from the blood.[6, 24] Flies, formerly incriminated as vectors, now appear to play a minor role as mechanical transmitters of the virus.[5, 17, 25] The organism that has been recovered from flies is human in origin.[4] Though flies have been known to disseminate virus, wholesale spraying of areas with DDT or fly-killing frosts have minimal effect in preventing outbreak of the disease.[11, 26] Virus is usually carried by a species of fly, *Phormia regina* (the filth fly).[17, 23] Mosquitoes are regarded as very unlikely vectors.[17]

Poliomyelitis epidemics do not follow the usual pattern of food or water outbreaks, which are explosive and affect masses of people simultaneously.[2] On the contrary, the epidemics build up gradually and show a radial type of development.[27] Usual methods of water sterilization are considered adequate.[4] Transmission of the virus by milk is unlikely, owing to the fact that pasteurization is general.[4, 27]

Though virus-contaminated fruits and vegetables have been ingested by monkeys without ill effect, this does not preclude this mechanism of transferral of virus to human beings and subsequent multiplication of the virus in the body of the host, producing clinical symptoms.[23, 25, 28] Toomey et al.[29] noted that "supernates of various fruits" injected into cotton rats predisposed them to a readier reception of poliomyelitis virus subsequently introduced.

The intimate contact by children at play, coupled with a natural inclination to avoid hand washing, may conceivably be the mechanism of transferral of fecal or pharyngeal contamination.[9, 23]

Droplet infection is still held by some to be the nature of virus spread in the genesis of some epidemics.[5, 27]

Authorities are now agreed that the human carrier, either healthy or with an abortive case, plays the major role in the spread of poliomyelitis.[5, 23, 27, 30] Whether poliomyelitis is spread by means of oropharyngeal secretions or the alimentary-tract excreta has not been conclusively settled.[15, 31] Those who favor the former method of dissemination base their conclusion on the observations that infection is transferred during the few days immediately prior to and after the onset of poliomyelitis[23] and that virus is found in high concentrations in the oropharynx during the first three to five days of illness[17, 32] and less frequently thereafter. In paralytic poliomyelitis the virus is not found in oronasal secretions after the first week.[17] These observers further noted that the infectious period for transmission of virus by personal contact is the short interval of three to five days after onset of the disease and that the virus is present in the stools of healthy, paralytic and nonparalytic persons for weeks after onset of disease.[23, 33, 34] This suggests that the contact medium is probably not the virus-infected stool.[4, 26, 35] Sewage during an epidemic is grossly contaminated with virus.[33] The theory of enteric spread is favored by the seasonal occurrence of the disease.[4, 32] Poliomyelitis virus, as well as intestinal toxins, according to Toomey,[36] accounts for entrance of disease by way of the intestinal mucosa. Some writers entertain the concept of a possible dual mechanism of spread: oropharyngeal secretions and feces.[30]

Portal of Entry

Twenty years ago experiments on monkeys appeared to demonstrate that the virus of poliomyelitis gained access to the body through the cribriform plate of the ethmoid and thence to the central nervous system. By instillation of copper sulfate solution the avenue of entrance was satis-

factorily blocked in rhesus monkeys.[17] Fortunately or not, this method of prophylaxis was not effective in human beings. The portals of entry into the body under review at present are: the skin, the olfactory apparatus and the gastrointestinal mucosa. There is no current evidence that the skin is the portal of entrance.[17] Conceivably, the skin, if denuded, might allow admission of virus,[36] though this is generally unlikely except experimentally. Present theories controverting the earlier nasal-route concept are that the season for poliomyelitis is not the usual one for upper respiratory infections,[17] no lesions are found in the olfactory bulbs[17] and chemoprophylaxis, which worked experimentally, was ineffective in human beings.[17] Experimentally, poliomyelitis has been produced in the cynomolgus monkey by ingestion of virus-containing food into the nontraumatized gastrointestinal tract.[37]

Toomey[26] suggests that the virus of poliomyelitis may travel up the gray fibers of peripheral nerves exposed to its action — whether via gray fibers exposed by denuded or inflamed epidermis or by mucous membrane. In such traumatized sites new vessels accompanied by additional gray fibers proliferate, thus producing additional axis cylinders for the transport of the virus.[36] Degeneration begins only when the virus has reached the nerve cell. This degeneration varies in degree as does the inflammatory responses that in large part account for the variability of signs and symptoms of poliomyelitis.[28] Bodian[28] observes that when marked inflammatory response occurs it usually follows destruction of anterior-horn cells, producing irreparable paralysis.

A few years ago the concept of anterior poliomyelitis involved principally that of a viral infection of the anterior horns of the spinal cord. This limited view is no longer tenable. Nerve-cell changes, with accompanying inflammatory reaction, occur in the reticular formation[38] and tegmentum of brain stem.[39] Cortical lesions usually involve only the motor area.[28] Bodian[28] states that the three areas in the brain most often severely damaged are the reticular formation, the vestibular nuclei and the roof nuclei of the cerebellum. Since the cerebrum has minimal involvement as compared with other sites, it is thought by investigators that lesions here are rarely, if ever, responsible for clinical symptoms. Lesions in the brain stem extending forward to the hypothalamus probably account for clinical manifestation of restlessness, drowsiness, disorientation and coma. Recently, centers of complicated somatic functions have been localized to the reticular formation. Lesions in this area are thought to explain the occurrence of difficulty in respiration, vasomotor control, swallowing and motor inhibitory activity.[28, 40] Much remains to be done in correlating the site, gravity and distribution of lesions in the reticular formation with clinical findings. The three common sites of lesions formerly noted are interconnected, and it is probable that their co-operative function is the modification of motor activities originating in the cerebral cortex.

It is quite generally agreed that the virus of poliomyelitis, on gaining entrance to the body, travels up an unmyelinated gray fiber until the spinal cord is reached. Here the large cells of the anterior horns are most severely damaged, with possibly less damage inflicted on the intermediate columns and least on the posterior horns. The virus is widely disseminated in the spinal cord at the onset of paralysis, notably at the cervical and lumbar enlargements.[41] It is postulated by some[28, 42, 43] that muscle weakness and spasm may no longer result alone from lesions affecting the anterior horns of the spinal cord, but may be due to lesions of the internuncial fibers. Lesions of these connecting fibers result in release of inhibition of proprioceptive impulses. This concept is based on findings in animal experiments demonstrating muscle spasm accompanying lesions of internuncial fibers but with quite normal anterior-horn cells.[16]

There is still conjecture about whether muscle paralysis results from extension from the central nervous system or by direct virus action on myoneural junctions.[44] Additional routes that have been considered are directly, via circulatory apparatus[14] and in a retrograde manner in the lymphatic vascular system related to the dorsal-root ganglions.[45] In the subacute and early convalescent period the extent of paralysis parallels quite closely the amount of nerve-cell damage. This does not hold true in the acute phase, in which other factors may contribute to the extent of paralysis.[28] Edema and inflammatory products at the site of the lesion may make the paralysis appear graver than it actually is.[28] In such temporary derangement of muscle innervation a degree of function will return with adequate therapy. At present there is no satisfactory explanation for the marked increase in the power of paralyzed extremities after the third month. The relative immunity of the cerebral cortex to poliomyelitis makes possible a happier prognosis, for the patient can in time relearn certain motor patterns heretofore directed by brain-stem centers.[28]

Factors in Immunity

There is growing hope that the paralysis of poliomyelitis may be controlled or prevented through some mechanism of immunity response (immunogenesis).[31] Clinically, several factors have appeared to influence the susceptibility of the host to the invading virus. Whether or not a given community will be the focus of a poliomyelitis epidemic is still not known.[5] It must be borne in mind that once a nidus exists the virus is widespread during the epidemic,[29] and some suspect

that the virus persists in the community subsequently.[5] It is estimated that for every recognized case of poliomyelitis there are a hundred others harboring the virus, with minimal or no symptomatology but with demonstrable antibodies in the blood.[46] Studies confirm the finding that several or all children of a household and sometimes adult members become asymptomatic carriers or subclinical cases of poliomyelitis, once a known case of poliomyelitis has developed in the family.[46] When multiple cases occur in a family 80 per cent of them acquire poliomyelitis within a week of each other.[47] It is thought that few if any proved cases of poliomyelitis result from school contacts.[27] In a study of poliomyelitis in an unsanitary rural area, Francis and Brown[48] found that few children were carriers on the first day of school and deduced that few infections occurred in persons not members of a group in rather intimate association with an actual case of poliomyelitis. Others have observed that 75 to 80 per cent of pools of family associates harbor the virus either in stools or oropharynx contrasted with 18 to 36 per cent of the nonfamilial associates.[30, 48] Second attacks of poliomyelitis are being reported with more frequency.[49] Virus was isolated from stools of apparently healthy carriers as early as 1913, and the number of reports of such isolation has been increasing since 1935.[30] Since 1945 there have been three reports of isolation of virus from stools collected during the incubation period.[50]

Another factor in resistance to the disease is general body well-being and freedom from exhaustion. In spite of the fact that preparalytic symptoms give no clue to the gravity of paralysis, it has been observed that a history of great physical exertion may precede the onset of severe paralysis.[51] Likewise, mental strain, such as that from driving a car over long distances, is equally ill advised.[52] It is concluded that physical and mental exertion during the prodromal phase may change what would ordinarily have been a mild or abortive case of poliomyelitis to one with paralysis, or may increase the amount and site of paralysis or, if exertion occurs after the preparalytic stage, may reprecipitate meningeal symptoms.[53]

Though pregnancy doubles the hazard of contracting poliomyelitis,[54] age, the number of pregnancies and the stage of pregnancy do not appear to be factors in susceptibility.[55] Better prognosis in the first two trimesters may be explained by the protection that estrogen and progesterone may lend. Lack of hyperemia and congestion of the upper respiratory and digestive tracts, as well as less fatigue at this stage of pregnancy, may be contributing factors.[54] Though the virus is not known to pass the placental barrier, poliomyelitis can be transmitted to the newborn.[55]

The present concept of the relation of tonsillectomy to poliomyelitis held by many observers is that the operation may change the carrier state of poliomyelitis into a clinical syndrome. When this occurs the extent of spinal-cord involvement is higher in the midbrain, producing the bulbar type of disease with greater mortality.[56, 57] Cunning,[58] in reporting a nationwide survey under the auspices of the American Laryngological, Rhinological and Otological Society, reviewed 5872 case reports of poliomyelitis (23 per cent of all cases reported in the United States in 1946), and found that 1.6 per cent had followed recent tonsillectomies. In the 1948 tonsillectomy-poliomyelitis survey, Cunning[59] expressed the conviction that "when bulbar poliomyelitis follows tonsillectomy it is coincidental." Experimentally traumatized areas in the gums, oropharynx or gastrointestinal mucosa may influence the incidence of infection.[41]

Eschenbrenner[60] states that since the oxygen requirement of the central nervous system is approximately thirty times that of other body tissue, anesthesia, with resultant anoxia, may disturb the delicate balance between the host and virus. Other "trigger mechanisms" may be a sudden change in body temperature, overexposure to sunlight,[58] overindulgence in carbohydrate-rich foods, acute infections and liver insufficiency,[61] and constitutional makeup.[58] Imbalance of hormones, with resultant disturbance of carbohydrate metabolism, may disturb the host-virus balance.[61] The hypoglycemia that may result increases susceptibility and contributes to the higher guanidine level, which is thought to increase spasticity of muscles.[61]

Considerable progress has been made during the last few years in research on the mechanism of immunity. Morgan[31] reports that a high level of neutralizing antibodies has been found in the serum of monkeys after repeated injections of active virus. Successful vaccination of monkeys with formalin-inactivated virus lends hope to the possibility that in the future a safe vaccine for human use will be developed.[31, 62, 63] Early experimental work with monkeys did not consider the possibility of different types of poliomyelitis virus, which present information reveals as three immunologic types[64] with fourteen strains.[31]

Two types of immunity are possible. The naturally acquired type occurs after exposure to the virus not followed by disease, whereas the passively acquired type has occurred after injection of adult human serum. The latter method has not been carefully evaluated by a human experiment.[31] Second attacks of poliomyelitis in the same person may be explained as caused by immunologically different types of poliomyelitis virus.[31]

Differential Diagnosis

The ability to diagnose a case of nonparalytic poliomyelitis with certainty even in an epidemic requires considerable clinical acumen, for the symptoms are protean and at present there is no

specific laboratory or clinical test that establishes the diagnosis.

In about 20 per cent of cases, poliomyelitis shows a diphasic course initiated by a generalized infection with nonspecific symptoms of fever, vomiting, headache and sore throat.[65] A symptomless period of approximately one to four days follows, terminating with the second phase of central-nervous-system involvement (meninges, brain and spinal cord) and with stiff neck, sometimes reflex changes and paralysis.[6]

Poliomyelitis may simulate the presenting symptoms of varied pathologic states, such as encephalitis[66] (including post-infectious encephalitides[67]), diphtheritic neuritis,[68] Guillain–Barré syndrome,[68] meningitis[49] (including lymphocytic choriomeningitis,[69] mumps meningitis[67, 70] and tuberculous meningitis[67]), infectious mononucleosis,[67] tick paralysis[67] and epidemic pleurodynia. Probably the commonest mistake is made in the differentiation of poliomyelitis from tuberculous meningitis.[65] A falling glucose level and low chloride should aid in the diagnosis of this type of meningitis. The scope of this paper does not permit detailed discussion of differentiation of the diagnoses listed above — they are noted to emphasize the fact that a typical case of poliomyelitis is not crystal clear.

There continues to be unremitting search for a specific test to aid in the diagnosis of poliomyelitis. Urinary excretions have been studied, showing that in man there is no significant alteration of 17-ketosteroids.[71] Creatine is excreted in large amounts in the urine of mice during experimental disease.[72] Dolldorf[72] suggests that potassium levels may also show appreciable alteration. Since there is a rise in neutralizing antibodies to poliomyelitis virus at the onset of paralysis[31] a type-specific serologic test would have practical value.[73]

At present there are no laboratory aids to the diagnosis of poliomyelitis except those furnished by the spinal-fluid changes. Recent verification of earlier noted spinal-fluid findings are as follows: the cell count is usually normal after the first week, but may rise to 20 to 60 per cubic millimeter later in the disease; mononuclear leukocytes are the predominant cell type, though polymorphonuclear leukocytes may be in ascendancy early in the disease[74]; cell counts may rise to 250 per cubic millimeter; and the protein is usually up to 40 mg. per 100 cc., the maximum rise occurring between the tenth and the thirty-fourth day.[68, 75] Half the 21 cases reviewed in one series showed protein elevations above 100 mg. per 100 cc.[68] These variations in spinal fluid are unpredictable, for in as many as 10 per cent of proved cases the spinal fluid has been normal.[74] The white-cell count and sedimentation rate are too variable to be of specific diagnostic aid.[65]

Types of Poliomyelitis

To understand more clearly the expected symptoms of the various types of poliomyelitis and their treatment in the light of present knowledge, a more workable classification of each type, with findings on history and physical examination, is presented in Table 1.[76] The diagnosis of the spinal form of poliomyelitis is made on the basis of the following findings, as given by Bennett[75]: acute onset of spotty segmental weakness, ranging from slight paresis to complete flaccid paralysis, with or without previous nonspecific prodrome of one to ten days' duration, no gross sensory changes (minor and transient paresthesias may be noted in the early stages), altered deep tendon reflexes in the involved segments, characteristic, but nonspecific spinal-fluid findings, with a moderate cell increase (50 to 250 per cubic millimeter) and moderate increase in total protein (50 to 150 mg. per 100 cc.). These may be accompanied by any combination and degree of motor involvement in medulla and midbrain.

Bulbar poliomyelitis is recognized with the help of the following symptoms[75]: acute onset of marked anxiety and restlessness, with weakness in muscles supplied by the cranial nerves, disturbances in the automatic control of breathing (jerky irregular respiration with variation in rate, depth and rhythm) or disturbances in cardiac function, consisting of very rapid pulse rate and varying blood pressures with decreasing pulse pressure or any combination of these signs, which may be accompanied by any combination of the lower motor neuron involvement of spinal cord, with or without characteristic spinal-fluid changes. Horstmann[76] further noted the following variations in young children: diphasic type is commoner under age of fifteen; onset is abrupt; interval between onset of preparalytic symptoms and paralysis is short; and superficial and deep pain is less.

Treatment

Through the years a variety of therapeutic agents have been suggested for poliomyelitis. To date no single specific treatment has been efficacious. The aim of all forms of therapy should be "to relieve pain, to minimize debility, to prevent and correct muscular deformity, and to treat the emotional disturbances which occur so frequently."[74] The final result depends on the teamwork of many specialists.[77] The purposes of this medical team of experts should be: utilization of all intact neuromuscular units, prevention or minimizing of all musculoskeletal deformities that would limit the most effective use of these units, training of patient and parents in their responsibilities within the program and intelligent acceptance of patient and family of ultimate physical limitations.[78]

Adequate care includes bed rest as soon as possible in a general[79] or communicable-disease hospital where the patient may be isolated and may have available all necessary mechanical equipment and skilled nursing and medical personnel.

On admission to the hospital the patient should be put in a hard bed with footboard placed several inches from the end of the mattress to protect the extremities from pressure and to allow stimulus of proprioceptive reflexes.

Moist heat has been advocated since the disease was first recognized.[80] Though this form of therapy a series of 79 cases of acute anterior poliomyelitis, gave symptomatic relief of pain and spasm in all cases.[89]

Lawson and Garvey[90] report that when Furmethide (furfuryl trimethylammonium iodide), a parasypatheticomimetic drug, is used catheterization may be avoided in most patients with urinary retention accompanying severe involvement of the lower extremities. Adult human serum has been found to date to produce no benefit in cases of poliomyelitis.[85, 91] In spite of a few favorable reports, serum from convalescent patients likewise

TABLE 1. *Classification of Various Types of Poliomyelitis.*

TYPE	SYMPTOMS	PHYSICAL FINDINGS
Abortive (symptomatically nonspecific, mild, brief illness without clinical evidence of central-nervous-system involvement)	Mild complaints occurring at time of epidemic in child, young adult or pregnant woman (other illness in family usually reported); later, elevation of cerebrospinal-fluid protein.	Listlessness, fever and redness of pharynx
Nonparalytic (clinical signs of central-nervous-system disturbance with nerve-cell damage not severe enough to produce weakness or paralysis):		
Diphasic: First phase, mild indisposition followed by brief period of well-being before second, more acute phase	Listlessness, fever, headache, sore throat (in absence of upper respiratory infection) anorexia, vomiting and, rarely, diarrhea	Same as those of abortive type
Second phase: Sudden onset	Fever, headache, vomiting, redness of pharynx (without sore throat), diarrhea or, more often, constipation, followed by spontaneous pain in extremities, soreness and stiffness of neck and back and pain in flanks and chest	Fever and dusky-red pharynx, with little or no edema of pharyngeal tissues; slight stiffness of neck, back and hamstring muscles; positive Hoyne sign of head drop; normal and active reflexes in early stage.
Gradual onset	Listlessness, slight and intermittent headache, anorexia, mild pains in extremities, with paresthesias and hyperparesthesias (slight stiffness of neck, back and hamstring muscles may precede fever*)	
Monophasic (essentially same as second phase without antecedent first phase, or with one so mild as to be unrecognized or so brief as to blend with second phase)		
Paralytic	Definite muscle weakness or paralysis	Reflexes change from normal to hyperactive and then shift to diminished or absent—superficial reflexes (abdominal, cremasteric and spinal) disappear about 1 day before paralysis is noted, with deep reflex changes before paralysis; paralysis of diaphragm and intercostal muscles in bulbar type.

*Other symptoms include psychic reactions, transient personality changes (such as irritability), convulsions in rare cases, dizziness (lightheadedness), shaking chills in rare cases and generalized tremulousness (last two occur more often in bulbar variety).

does not alter the course of paralysis, it adds greatly to the patient's comfort, aids in preventing and correcting deformities and assists in development of full range of motion. Hot baths may be used for children, but hot moist packs, according to the Kenny[81] method, are most effective in relieving the pain.[76, 82]

Analgesics such as aspirin and Demerol are helpful to relieve pain.[31] Narcotics should be used with caution if the patient is not already in the respirator.

Penicillin is advocated for respiratory cases since there is the added hazard of upper respiratory infections.[84, 85] Among the newer drugs used to relieve pain and relax muscle tightness is Prostigmine. This drug has not enjoyed united approval.[31, 82, 86] Curare likewise has had an equivocal reception.[82, 87, 88]

Procaine hydrochloride, Priscol hydrochloride and diethylaminoethanol hydrochloride, used in has not been established as effective treatment, once the preparalytic state has been reached.[92, 93]

Additional problems of management arise in the treatment of bulbar or respiratory involvement necessitating use of the mechanical respirator. The chief aim is to save the patient's life. An "unobstructed airway, administration of oxygen suction of pooled fluids in hypopharynx, and adequate hydration and nutrition"[74] are required. Patients must not be placed in mechanical respirators unless the respiratory tract is unobstructed.[94] It is essential that anoxia be prevented. Tracheotomy should be performed when difficulty in breathing first develops. This distress may be recognized by the observation that it is usually accompanied by acceleration of the pulse. A tracheotomy should be done preferably before the patient is placed in the mechanical respirator. Peterson and Ward[95] described a new type of apparatus called

the "collarless" respirator, which obviates the difficulties of doing a tracheotomy that have arisen in the conventional type of respirator. Use of a cam-driven bellows on the respirator provides a more normal type of respiration and adds to the patient's comfort.[65]

The tracheotomy tube should be aspirated[96] as need requires, and the tube should be maintained in position as long as the patient needs an airway. Criteria for removal of tracheotomy are satisfied when the patient does not need an airway and has not had to be "suctioned" for a week.[84] Oxygen under positive pressure may be supplied by a mask. The vital capacity of the patient both in and outside the respirator and the tidal air in the respirator may be used as checks or possible overventilation and underventilation of the patient.[84]

Phrenic-nerve stimulation (Sarnoff) has not been widely evaluated. This technic may have diagnostic value as a check of the ability of the diaphragm to contract.

The oximeter for measuring the change in saturation percentage of oxyhemoglobin in arterial blood is advocated by some clinicians.[31, 85, 97]

In summary, Brown and Baker[97] outline the following guides in the handling of bulbar cases: early elective tracheotomy; adequate suction of pharynx and tracheotomy; oxygen mixtures up to 40 per cent under positive pressure if pulmonary edema is expected; adequate humidification of gas mixture; careful checking of the oxygenation of the patient by means of arterial oxygen determinations and use of oximeter; frequent moving of the patient to avoid hypostasis and thrombophlebitis; maintenance of nutrition by nasal feeding; penicillin prophylactically; avoidance of sedative drugs and use of stimulants; early closure of the tracheotomy; and unceasing watchfulness on the part of the doctor and special nurses, in the realization that mechanical devices are far from foolproof.

The oscillating bed (respir-aid rocking bed) allows the patient more freedom and facilitates nursing care.[77] The viscera press against the diaphragm, helping exhalation, and as the bed swings in the other direction inspiration is aided as the viscera tend to fall away from the diaphragm. Some patients tolerate this treatment well. One advantage of the oscillating bed is that it allows some patients to remain out of the respirator for four or five hours when without it they could remain out only a few minutes.[84] The bed does, for an unexplainable reason, produce a greater secretion of mucus in the respiratory tree in some cases.

Aftercare is a prominent part of the present concept of the total management of cases of poliomyelitis. All patients with muscle involvement should be under the care of "someone skilled in the care of the skeletal system from the very start of the disease."[98]

Precise muscle examinations are required with indicated follow-up care of graded exercise[82] and stretching of muscles when contractures have occurred.[98] Even in late cases muscle strength may be improved by progressive resistance exercises.[99]

Orthopedic surgery for permanent misalignment will depend on the recovery-rate expectancy curve and the patient's age.[78, 100]

Whether circulatory changes are due to direct damage to autonomic ganglions or secondary to inactivity remains a question yet unsolved according to Buchthal.[38] Collins et al.,[101] in a study of 131 convalescent cases, noted that vasomotor disturbances, such as coldness and sweating, as well as spasm, were relieved by paravertebral sympathetic block with 2 per cent procaine. Since block of the sympathetics relieved muscle spasm and tenderness, which, they observe, persisted for several months, they conclude that impulses producing pain and spasm are "mediated in part by the sympathetic system."

Neurotripsy has been a fairly recent addition to the aftercare of these patients. As explained by its originator, Billig,[102] the aim is to increase the power of muscles with residual paralysis by injury to the nerve. This is accomplished by crushing of the nerve after surgical exposure or by forceful manual massage of the muscles. The nerve during regeneration produces axon branches, which in the end furnish more innervation to the weakened muscle.[102] Checking the effects of neurotripsy as advocated by Billig, Hodes[103] noted abolishment of the neuromuscular block after treatment and agreed that this is a "possible useful therapeutic procedure in the treatment of poliomyelitis," though others[82] do not concur in his opinion.

Care of the patient with poliomyelitis should include careful check of the heart, since involvement of the sympathetic nervous system may manifest itself in the thoracic region by spasm of the pulmonary blood vessels, with dilatation and irregularity of the right side of the heart.[104] Ludden et al.[105] found 14 cases of myocarditis in 35 autopsies. They believe that lesions of the heart may be caused by the same virus that produces poliomyelitis. Psychotherapy should be included in the armamentarium of therapeutics for cases of poliomyelitis.[82] There is little to show that changes in electroencephalographic tracings are marked enough to produce any behavior manifestations.[106] Authorities agree that the panic engendered by poliomyelitis onset, the long nature of the process and the fact that the disease often attacks young persons point up the need for psychiatric therapy from the onset of the acute stage throughout convalescence and rehabilitation.[74, 100]

Superstitious fear rampant among the laity when poliomyelitis strikes in a community must be dispelled by education and reassurance. Here the medicosocial workers may be of great aid in allaying

needless fears and helping the patient adjust himself to his particular future possibilities.[107]

The care of the patient is not complete when the optimum in musculoskeletal function has occurred. There must be physical rehabilitation and, if possible, the learning anew of skills that the patient may be returned to his community with a modicum of security psychologically and economically. To have the powerlessness of infantile paralysis lifted, stated Franklin Roosevelt, "means the difference between a human being hopelessly dependent on others — and an individual."[5]

Van Riper[108] summarizes the situation as follows:

> Acute anterior poliomyelitis demands of the physician and his professional co-workers the same exercise of judgment in the administration of therapeutic measures as does any other acute infection. He must consider the patient first, the disease as secondary in importance.

Control

People have a unique dread of poliomyelitis, largely based on the inborn fear of the unknown.[8] Its etiology is unknown. The onset is dramatic and unheralded, and the outcome is unpredictable. Its effects are often irreversible.[107] This attitude held by the public must be met by a forthright management of the problem in the light of present knowledge of poliomyelitis, limited as it is. When possible, the public-health officer should serve as the source of education for the physician as well as the laity. In this education the aim should be accuracy of information and relief of fear and anxiety.[79] Latest data on poliomyelitis should be possessed by the doctor before the public receives similar information from the press, radio, clubs and television. Citizen committees to meet the peculiar needs of an afflicted community may work with personnel of the medical profession to accomplish much during an epidemic.

The public should know that of 100 exposed persons, symptom free but harboring the virus, actually only 1 suffers a clinical attack.[108] Also, of those exhibiting clinical manifestations of the disease, only a small percentage are left with crippling sequelae. Education in the care of patients in the preparalytic stage will not stop an epidemic once begun, but may prevent paralysis.[23] There is no method as yet devised for the control of poliomyelitis, for questions about what initiates an epidemic, the mode of entry into the body, the method of spread and the reason for subsidence of occurrence, with many others, have not been answered. The following methods of control have been suggested: the closing of motion-picture theaters and churches, and the refusal of admission of patients to general hospitals is unnecessary[31]; proper isolation technic, which will protect patients and personnel from exposure to known cases[5]; closing of swimming pools and playgrounds, since present information suggests that the virus is transmitted by direct contact of persons[23]; avoidance of exhaustion since various observers cite cases of paralysis following excessive physical exercise[23]; mass spraying with DDT is not recommended.[23]

If a patient must be cared for at home, isolation is best for two to four weeks, with the longer period preferable.[23, 85] Horstmann et al.[34] found that in 61 patients after acute poliomyelitis, virus persisted in stools in 50 per cent for five or six weeks. In only 1 case was virus present in the twelfth week.[34] Cases of poliomyelitis do not produce chronic carriers as typhoid does.[34] Children and food handlers from such "infected homes" should remain at home for two weeks.[23] The incubation period has a wide spread of four to thirty-five days.[77]

In addition to the above suggestions, the following may well be added: placing of emphasis on hygienic measures by thorough washing of the hands after toilet and before meals; avoidance as much as possible of close-contact play activities among children if an epidemic is present — since throats have not been ruled out as potential sources of infection[32]; vigilance in avoiding any mechanical transmission of virus by flies and so forth to food; pasteurization of milk (water should be obtained from a reliable source)[36]; thorough washing of fruits and vegetables[36]; and avoidance of constipation.[36]

Research

As summarized by Toomey,[36] the most important events in poliomyelitis research are: isolation of virus from human beings and transfer to monkeys; demonstration of virus-neutralizing antibodies in the blood serums of patients convalescing from poliomyelitis; evaluation of the pathology of the disease and acceptance of the conception that nerve cells are destroyed first and that other phenomena follow; demonstration that virus spreads along neurons to the central nervous system; discovery that the virus can be acclimated to some smaller laboratory animals; and demonstration that the virus can be easily isolated from the stools of patients who have had the disease.

Recently, the virus has been isolated in almost pure form.[109] The National Foundation for Infantile Paralysis, which was formed in 1938, has carried on a nation-wide program of research, education, epidemic aid and medical care. Hart E. Van Riper,[108] medical director, has noted the following major problems to be solved if preventive or curative measures are to be implemented; the development of a simple laboratory test to identify, preferably, a single virus particle; development of a simple diagnostic laboratory test to indicate whether or not infection with the virus has taken place; determination of the relative number of virus particles required to infect the human being and the laboratory animal; determination of the physical, chemical and biologic characteristics of the virus particle; determination of the number and characteristics of the different types of the virus that

produce clinical disease in man; and development of a full understanding of the metabolism of the cell and of the virus, and of how the metabolism of the virus interacts with the metabolism of the host cell to produce disease.

In summary, poliomyelitis is no longer a purely "infantile" disease. Though the causative organism is a virus, more research remains to be done on the various types of viruses. A single mode of transmission has not been agreed upon by investigators. The nasopharyngeal, as well as the gastrointestinal, portal of entry has its advocates. Immunity factors, though complex, show that the direct human contact is probably the weightiest circumstance in determining the onset of the disease. An important contributory factor in prevention of poliomyelitis and in minimizing paralytic complications is general well-being and freedom from exhaustion. The differential diagnosis is difficult and is often confused with that of tuberculous meningitis. No "specific" diagnostic aid has been found to date. Treatment for poliomyelitis continues to be multiple in type. Refinements for care of respirator cases are constantly appearing.

Though great strides have been made in elucidating the complexities of this ubiquitous disease, many hurdles remain. Research continues in several medical centers on the improvement of technics for care of respirator cases, which have the highest death rate.[19, 110] Hope is expressed by some workers that a drug, specific for poliomyelitis, will be discovered.[104] New developments in the recognition of poliomyelitis occur continuously, such as the isolation by Melnick et al,[111] of a new virus that produces clinical findings simulating the mild form of poliomyelitis. In a review of the fifty years since the appearance of poliomyelitis in epidemic form in this country, it is evident that a fair number of the inscrutable mysteries formerly surrounding poliomyelitis are surely being solved. From continuing research and clinical investigation, one takes renewed faith and hope that the problems still surrounding this disease will be solved — that in the imminent future men, women and children need no longer bear the crippling stigma of poliomyelitis.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 36231

PRESENTATION OF CASE

An eighteen-year-old girl was referred to the hospital for further investigation of abnormal shadows reported in a routine chest survey x-ray examination.

Two years prior to admission the patient first noticed a swelling on the left side of the neck. She had discovered it while in the bathtub and made the comment that she believed it became more prominent when the area was warm. It was never tender or painful, and she thought there had been no change in size although possibly it had been located farther toward the back of the neck when first noticed. There had been no cough, hoarseness or dysphagia. The patient had observed that she was tired and somewhat out of breath after climbing stairs. This had become more noticeable during the past three months, along with a generally increasing fatigability and a feeling of heaviness in the eyelids, which she overcame by closing the eyes for several minutes.

Ten years prior to admission an asymptomatic goiter was removed at another hospital. Three years before admission she had been admitted to still another hospital after the eighth and most severe episode of swelling of the face, hands and feet with itching and a "blotchy red" rash. She had a fever of short duration and after some "injections" was discharged home after one week. Since then she had no similar recurrent episodes. She had been overweight since the age of twelve years without recent change and always had a preference for cold weather.

Physical examination revealed a well developed but generally obese young woman. An old thyroidectomy scar was present. In the left supraclavicular triangle there was a soft, nontender, movable, smooth mass about 4 by 3 cm. that seemed to disappear below the clavicle. It transilluminated and was observed to enlarge perceptibly after the application of a hot towel. It did not move on swallowing or coughing, nor was any pulsation or bruit discernible. The trachea was deviated to the right. At the left apex there were dullness, tubular breath sounds and decreased tactile and vocal fremitus. There was some tenderness to firm pressure over the third, fourth and fifth ribs along the left sternal border. There was no lymphadenopathy although several submaxillary lymph nodes were palpated by one observer. A Grade II apical systolic murmur was heard in the heart, with the apex at the midclavicular line. The left radial pulse was recorded as weaker than the right by one observer. The deep tendon reflexes were hypoactive but equal throughout.

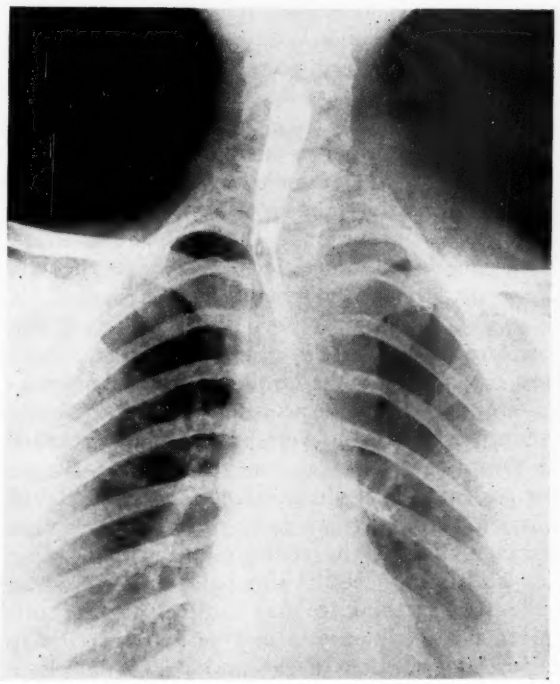

FIGURE 1. *Barium-Swallow Examination of the Esophagus. A soft-tissue fullness in the left side of the neck displaces the esophagus to the right.*

The temperature, pulse and respirations were normal. The blood pressure was 105 systolic, 70 diastolic.

The hemoglobin was 12.0 gm., and the white-cell count 7700, with 79 per cent neutrophils. The urine was normal. The blood cholesterol was 230 mg. per 100 cc. Determinations of the basal metabolic rate were −12 and −15 per cent. The chest films and the film taken following a barium swallow showed a soft-tissue mass in the left side of the neck extending down to the level of the clavicle and deviating the trachea and esophagus to the right (Fig. 1). Another portion of the mass extended

downward into the left superior mediastinum and overlay the aorta. The mass did not move on swallowing. There seemed to be some compression of the trachea, but the lungs were clear. The heart, diaphragm and bones were not unusual.

On the tenth hospital day an operation was performed.

Differential Diagnosis

Dr. Felix G. Fleischner*: I will attempt to approach a diagnosis by first reviewing the evidence that we see here in the x-ray films and that I shall demonstrate. There is a rather large mass in the neck on the left, and another mass in the mediastinum, also on the left. When we study the soft-tissue structures we see on the right side normal-appearing subcutaneous fat, the shadow of the trapezius and the levator scapulae and this fat layer in between, whereas on the left these landmarks are blurred. If one looks closely at the shadow of the left trapezius, one has the impression that it is not as homogeneous as the right and looks as if something were infiltrating it. I have the impression that I can even see the elevated superficial fascia. The mass is not too well defined. The trachea is displaced and slightly compressed. The apical pleura is depressed. We do not see any abnormalities, erosion or involvement of the ribs or transverse processes of the vertebras. It is fortunate that the patient was eighteen years of age. In an older patient one would consider the possibility of aneurysm. However, we have other proof against aneurysm, in that the contour of the descending aorta is distinctly seen at this point and is covered by the mass. I think we may assume that the soft-tissue mass is adjacent to and perhaps enveloping the posterior portion of the aortic arch. I would like to ask Dr. Wyman if there was any pulsation of the mass.

Dr. Stanley M. Wyman: I do not know, since I did not see the patient.

Dr. Fleischner: Any pulsation visible could as well be transmitted from the aorta. We note that the anterior mediastinum, which we see in the lateral film, is not the site of the mass, and this, of course, is of importance.

From the radiologist's observations we can discard quite a few of the lesions that occur in the neck. Since there is no connection with the salivary glands, particularly the parotid gland, we can discard the possibility of a cyst or tumor arising from those glands. The location of the mass and its extension beneath the skin rule out different types of congenital cysts such as bronchogenic cysts. A thyroglossal cyst in the midline, of course, cannot produce such an x-ray picture. There are many rare pathologic conditions that may explain either the lesion in the neck or the lesion in the mediastinum but there are very few that will explain both as one entity. From the examination of these films alone I believed that the mass might be a malignant lymphoma. The only other lesion I would consider is a hygroma.

Let us go back to the patient. Three years prior to admission, she noticed a swelling that had not changed. Since she was young and her general health was good, we may assume that there was probably not a malignant lesion. However, we must remember that thyroid cancer may occur even in the second or third decade of life, but one would not expect a lesion of the thyroid gland to extend into the mediastinum in this fashion. The patient noticed that this lesion became more prominent when she was taking a hot bath, and on physical examination the lesion became perceptibly larger when heat was applied. This calls attention to the possibility that the mass was a vascular tumor that started back in the lateral portion of the neck. Then we are given what I think is contradictory information. The patient had observed herself to be tired, and this became worse through the months preceding admission to the hospital. She was overweight. She had a preference for cold weather. The cholesterol of 230 mg. per 100 cc. was at the upper limit of normal, and the determinations of the metabolic rate, −12 and −15 per cent, were low normal too. There was nothing very definite. I do not know how to put this together.

There were no signs of retarded growth, sluggishness or impaired mental development. The drooping of the eyelids makes one think of myasthenia gravis. There was no thymic tumor, and I do not know how these masses we see in the neck and mediastinum were related to this symptom. I wondered for a time if it could have been an incomplete Horner syndrome. I do not see any extension of the lesion to the other side, and there was no evidence that anything developed on the other side. I have no explanation for it.

Two years prior to admission a goiter was removed. May I ask if this scar is described as across the neck or only on the left side?

Dr. Tracy B. Mallory: There was no note on the exact character of the scar.

Dr. Fleischner: We may assume for the time being that the patient had an asymptomatic goiter. We do not know whether or not she was from a goitrous section of the country, nor do we know the histology of the goiter; therefore, I cannot comment on that.

Then she had a skin disease, — eight episodes of swelling of the face, hands and feet, with itching, rash and fever, — which was relieved by a few injections and did not recur. I confess frankly that I am not too familiar with skin diseases, and therefore I asked Dr. Joseph Goodman to help me out. He replied that the description was too fragmentary to make a definite diagnosis, but that he would consider the possibility of erythema multiforme

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and could not rule out an eruption due to drugs or even a contact dermatitis. Apparently, this skin lesion had nothing to do with the diagnosis, however.

On physical examination the mass was 4 by 3 cm. in size. I think the most important point is that it transilluminated well. Transillumination means a cystic formation with nonopaque fluid. There are two lesions that may transilluminate: dermoid cyst and hygroma. It is said that hygroma transilluminates better than dermoid cyst, and furthermore a dermoid cyst will not explain masses in both the neck and the mediastinum. The mass apparently enlarged perceptibly after the application of heat. A solitary cyst would hardly do that, and hygromas are not, at least according to some pathologists, simple cystic lesions but some kind of lymphangioma in which there are cystic areas and also capillary and cavernous parts, which may explain this vascular phenomenon. There was apparently no close relation or close adherence to the trachea. There was no movement of the mass on swallowing.

A systolic murmur was heard over the heart. The heart appeared normal in size and shape in the anteroposterior and lateral views. Whether there was a mitral lesion or not we cannot decide. In any event it probably had nothing to do with the main disease. The left radial pulse was weaker according to one observer. It is quite possible for any mass in this area to compress the left subclavian artery. As we know, some tumors may cause such pressure only when the head and the shoulders are in certain positions, so that it is quite possible that one observer found the patient in that particular position and found a weaker pulse on the left side.

We have still to discuss the possibility of a malignant lymphoma. For the two years in which this mass was observed, it did not change. There were no general systemic signs or symptoms of any kind to suggest a malignant growth. I think we can discard this sort of tumor. There are some other possibilities that we may discard. We do not see any relation to the normal location of the thymus. One may think of neurofibroma, but practically all the other solid tumors are ruled out by the definite statement of transillumination.

There is one more lesion that I should mention. When I looked up the literature I found a case in which a young man was operated upon with a diagnosis such as this and cystic dilatation of the thoracic duct was found. The surgeon stated that aspiration yielded typical chyle and that the wound was closed without otherwise disturbing the lesion, since excision might have been disastrous. It is possible that such a mass developed from the thoracic duct in this case.

When we consider the possibility of cystic hygroma there is one difficulty. Most of these lesions occur immediately after birth or during childhood. The statistics presented by Gross and Goeringer[1] state that 50 per cent of cases are noticed at birth and 90 per cent within the first two years. On the other hand, of 14 cases reported from the Memorial Hospital,[2] 11 were noticed at birth, and the remainder at the ages of four, five and fifteen. There are reports that hygromas have been observed in adults. Perhaps this thyroidectomy was not for a goiter but for a hygroma, which was not radically removed. It is known that such tumors, if not radically removed, may recur even after a long time.

Dr. Neuhauser, of the Children's Hospital, has shown us repeatedly cases of mediastinal masses that were extensions of hygromas in the neck. In the report of the Memorial Hospital[2] 2 out of the 14 cases showed extension into the mediastinum. Now this would fit perfectly well. I would assume that we are dealing here with cystic hygroma or, if you prefer, a cystic cavernous and papillary lymphangioma of the neck with extension into the mediastinum. All the signs and symptoms seem to conform to that diagnosis.

Dr. Saul Hertz: I would like to ask one question about the disposition of the carotid artery about this mass. Some years ago I was interested in the differential diagnosis of tumors in this area. On the basis of some anatomical studies I was able to show that if the carotid artery is displaced medially the chances are that we are dealing with a neurofibroma in this area whereas if it is displaced laterally other types of lesions have to be considered. If it was not known clinically where the artery was, I wonder if the surgeon could tell us.

Clinical Diagnosis

Cystic hygroma.

Dr. Fleischner's Diagnosis

Cystic hygroma.

Anatomical Diagnosis

Lipoma of mediastinum and neck.

Pathological Discussion

Dr. J. Gordon Scannell: This patient was operated upon by Dr. Churchill, who used a new cervicothoracic approach that he is developing. A collar incision was first made, and the lipomatous nature of the mass determined. It could then be seen that the mediastinal extension called for greater exposure than was possible through the cervical incision. Therefore, a midline incision curving laterally in the left inframammary fold was made over the sternum, and the superior mediastinum widely exposed by splitting the sternum down to the third interspace and extending the incision well out into that interspace.

The lipoma was irregular, with many finger-like extensions. One of these passed behind the internal

jugular vein but anterolateral to the common carotid artery and vagus nerve and descended deep to the mediastinal pleura to the level of the pulmonary artery. Another mass lay in the posterior cervical triangle on the surface of the scalenus medius and levator scapulae muscles. Still another pseudopod of the lipoma had found its way to the paravertebral region through an ostium at the anterior border of the scalenus anticus muscle.

The exposure was admirably adapted to the resection of this tumor because it received its blood supply at several different points on its surface. The operative approach seems radical for a benign tumor, but actually this approach divides no muscles except the sternohyoid and the omohyoid. To have confined the approach to the cervical route would probably have meant, in addition, the division of the sternomastoid muscle, and perhaps the sacrifice of the internal jugular vein.

The patient was discharged on the seventh postoperative day.

A PHYSICIAN: Does the tumor look as if it might have transilluminated?

DR. MALLORY: It was composed of clear, bright-yellow fat; it was not to any great extent fibrous as lipomas occasionally are. I think the astonishing thing is that it proved as dense as it did to x-ray penetration. One might reasonably have expected a decrease in density rather than an increase.

DR. ALFRED E. KRANES: Would it have been necessary to do such an extensive operation if the nature of the tumor had been recognized?

DR. MALLORY: Lipomas may or may not continue to grow in size. If this had continued to grow, its relation to the great vessels might eventually have caused an upper mediastinal syndrome that would have been quite significant in producing disability.

DR. FLEISCHNER: How did it increase in size with heat? That was observed not only by the patient but also on physical examination.

DR. MALLORY: There are a moderate number of blood vessels in a lipoma. I suppose there could have been enough to increase the size of the tumor.

DR. FLEISCHNER: Is the nature of the thyroid operation now disclosable?

DR. MALLORY: Yes. We were able to get a report that it showed a fetal adenoma.

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CASE 36232

PRESENTATION OF CASE

A sixty-nine-year-old farmer entered the hospital complaining of shortness of breath on exertion.

At the age of thirteen the patient had an attack of St. Vitus dance that lasted about three months and was accompanied by an episode of intermittent painful reddening and swelling of the knees and ankles lasting two or three weeks. He was then well and able to do heavy labor as a blacksmith for most of his adult life. He had taken digitalis because of a cardiac arrhythmia for at least fifteen years prior to admission. Eleven years before admission he noted numbness and coldness of both feet. The dorsalis-pedis pulses were found to be absent bilaterally. Ten years prior to admission there was an attack of polyarticular pain and swelling accompanied by a slight fever. Following that episode the patient began to have exertional dyspnea accompanied by substernal pain that did not respond to nitroglycerin. Seven years before entry there was an attack of paroxysmal nocturnal dyspnea and cough productive of frothy, mucoid sputum. This responded to an injection of morphine and aromatic spirits of ammonia. For four years before entry the patient complained of pain between the shoulder blades occurring during dyspneic attacks and relieved by massage. Three months before entry there was a marked increase in dyspnea and onset of orthopnea requiring five pillows for relief. Two months before entry paroxysmal dyspnea occurred twice a night. During the week before admission there was a persistent cough productive of thick, mucoid, frothy sputum.

Physical examination revealed an asthenic, cyanotic elderly man. The neck veins were flat, and there was no edema. A few sticky, inconstant and post-tussic rales were heard, but the chest was otherwise clear and hyperresonant. The heart was enlarged to the anterior axillary line on percussion. The aortic second sound was louder than the pulmonic. There was a Grade III systolic murmur at the apex transmitted to the base and heard over the entire precordium. There was a suggestion of a low-pitched apical diastolic murmur with the patient recumbent and semirecumbent; in the left lateral position, it seemed fairly definite. The first sound was sharp. The rest of the examination was negative.

The temperature was 98°F., the pulse 92 and grossly irregular, and the respirations 24. The blood pressure was 130 systolic, 80 diastolic.

The urine had a specific gravity of 1.030 and gave a + test for albumin, and the sediment contained abundant bacteria and occasional hyaline casts. Examination of the blood showed a hemoglobin of 14.4 gm. and a white-cell count of 9900, with 55 per cent neutrophils, 35 per cent lymphocytes, 7 per cent monocytes and 3 per cent eosinophils. A stool was guaiac negative. The sedimentation rate on admission was 30 mm. per hour. An electrocardiogram showed flutter fibrillation at an average rate of 80, with the T waves upright in Leads 1 and 2 and inverted in Lead 3, with sagging ST segments. The chest leads showed upright T waves in Leads V_1, V_2, V_3, V_4, V_5 and V_6, with sagging

ST segments in Leads V_5 and V_6. The QRS amplitude was high in Leads V_5 and V_6. A chest x-ray film demonstrated a cardiothoracic ratio of 17.5:28. The heart was enlarged to the left, and there was prominence of the left auricle. The pulmonary vessels were engorged at the lung roots bilaterally and to a less extent in the parenchyma. The aorta was tortuous, with calcification of the transverse portion. The right leaf of the diaphragm was elevated, and there was a small amount of fluid at the right-lung base.

The patient was given 10 mg. of morphine sulfate on admission and put on a low-salt diet with ammonium chloride (1 gm. four times a day) and digitoxin (0.15 mg. four times a day). For the first four days of the hospital course he had no complaints other than a slight cough. He then had a sudden, marked deepening of cyanosis and moderate increase in dyspnea not accompanied by pain of any description. The temperature rose rapidly to 103°F., and the pulse to 102. On the day after the episode the white-cell count was 14,600, with 68 per cent neutrophils; three days later it was 25,500, with 85 per cent neutrophils. The sedimentation rate rose to 44 mm. per hour. A blood culture yielded *Staphylococcus albus*, believed to be a contaminant, and sputum culture yielded alpha-hemolytic streptococci and colon bacilli overgrown with *Proteus vulgaris*. The nonprotein nitrogen was 56 mg. per 100 cc., the sodium 137.0 milliequiv., the chloride 100 milliequiv., the bromide 12 milliequiv., and the carbon dioxide 23.2 milliequiv. per liter, and the prothrombin time 20 seconds (normal, 18 seconds). A single film taken at the bedside and marred by motion showed homogeneous density of the upper fourth and an apparent decrease in vascular markings in the remainder of the right lung. The patient was given oxygen by mask, as well as penicillin and morphine sulfate, with no clinical improvement. On the seventh hospital day there was a small hemoptysis. On the morning of the eighth day the blood pressure had fallen to 90 systolic, 60 diastolic and the patient was acutely ill. In the course of the day the chest filled with rales, and the blood pressure fell to 70 systolic, 40 diastolic. The apical pulse rose to 150 with a radial rate of 85. The patient failed rapidly and died that evening.

Differential Diagnosis

Dr. Gordon S. Myers*: I shall begin by saying what I believe this patient had, and then I shall try to justify my diagnosis. I believe that he had rheumatic heart disease with mitral stenosis and regurgitation, and possibly aortic stenosis as well, long-standing auricular fibrillation and congestive heart failure and multiple emboli to both the legs and the lungs, and that the final event was a massive embolism or possibly thrombosis of the right pulmonary artery, with some infarction of the upper portion of the right lung.

There are some points of interest that I should like to bring out in the history. This patient had rheumatic fever beginning at the age of thirteen. It was notable that he also had chorea at that time, and chorea is usually a favorable sign early in the course of rheumatic fever. That was borne out by the patient's uncomplicated career for many years without serious evidence of rheumatic disease. For about fifteen years prior to admission he had taken digitalis for cardiac arrhythmia. It is fairly likely that the arrhythmia was auricular fibrillation, which he had had for a long time and which was present when he came to the hospital. Eleven years before admission he had sudden numbness and coldness of both feet, after which dorsalis-pedis pulses were found to be absent and I think that episode probably represented emboli to the arteries of the legs.

Ten years before admission, when the patient was fifty-nine years of age, there was an attack of polyarticular pain and swelling accompanied by a slight fever. Although a patient of fifty-nine is rather old to have active rheumatic fever, we know that the disease can occur at any age. There have been reports of first attacks occurring at the age of sixty or over. Whether they were actually first attacks or not it is, of course, difficult to say. In some cases such episodes have been confirmed as active rheumatism by post-mortem examination with the finding of Aschoff nodules. Following this attack of what I presume was active rheumatic fever there was more evidence of cardiac disability in that the patient had increasing exertional dyspnea. Accompanying this was substernal pain coming on with exertion and not relieved by nitroglycerin. Later on we are told that he had pain in the back between the shoulder blades, relieved by massage. I cannot very satisfactorily explain this sort of pain but we have seen it in a number of different kinds of patients. Dr. Bland,† at one of these meetings, discussed a case of recurrent pulmonary emboli and death from cor pulmonale, with this type of discomfort coming on with exertion. I do not believe that I understand the pain. It does not sound like coronary-artery disease, and I doubt if this patient had angina pectoris.

Three months before entry there was a marked increase in dyspnea and onset of orthopnea requiring five pillows. It seems that something must have happened at that particular time: whether there was more active rheumatism, pulmonary emboli, as I suspect, or some kind of infection, I do not know. Suffice it to say that the patient had a rather sudden increase in pulmonary congestion. Finally, he entered the hospital in rather poor shape.

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†Case Records of the Massachusetts General Hospital (Case 35432). *New Eng. J. Med.* **241**:669-673, 1949.

It is of interest that, although the patient was cyanotic on physical examination on admission, the respirations were only 24, and the chest was clear and resonant aside from a few sticky, inconstant rales. That would be a little unusual for a patient who had a straightforward left-sided failure. It is true that one can have considerable dyspnea; even paroxysmal dyspnea of severe degree can occur with very little heard in the chest although on x-ray examination considerable pulmonary congestion may be evident. A physical examination of the heart was unsatisfactory as far as deciding whether or not aortic stenosis was present. There was a Grade III systolic murmur at the apex transmitted to the base and heard over the entire precordium that might have been due to mitral regurgitation. However, because of the appearance of the electrocardiogram later on, I wondered if this patient might not have had aortic stenosis as well. It would have been interesting to know whether or not there was a thrill in the aortic area and whether the systolic murmur was well transmitted up the vessels of the neck. In any case there were signs perfectly consistent with rheumatic heart disease and with mitral disease.

The examination of the urine was not too remarkable. It was said that there were abundant bacteria. Since we do not know whether this was a voided specimen or a catheterized specimen, I do not think we can make too much of it. There was a good specific gravity and a + test for albumin. Perhaps the patient had some minor degree of kidney disease, or perhaps he had old infarcts of the kidneys. Later on we find that the nonprotein nitrogen was a little elevated.

The electrocardiogram suggests to me the possibility of left ventricular hypertrophy more than anything else. It certainly is not characteristic of mitral stenosis. There is no evidence of right ventricular hypertrophy. The description of the initial chest x-ray film fits in with rheumatic heart disease and mitral involvement. The pulmonary vessels and the lung roots were engorged bilaterally, and there was a little fluid at the right base, so that this patient had some degree of congestive heart failure. Apparently, there was no indication of past pulmonary emboli or old pulmonary infarction. The patient had been fairly well in the hospital until the final episode of deepening cyanosis and gradual increase in dyspnea not accompanied by pain. Of course, that can perfectly well occur in the presence of a massive pulmonary embolism. Usually, such patients have some kind of substernal oppression or actually have a syncopal attack at the time of the embolism, but they do not complain of any pain until after pulmonary infarction has occurred. After this episode the temperature rose and the white-cell count was markedly elevated, which I think went along with the infarction of the upper pole of the right lung. The carbon dioxide at that time was a little low, perhaps an acidosis of renal origin since the patient's kidneys were not functioning very well.

The single film taken at the bedside is very suggestive of a massive embolism to the right pulmonary artery. It showed homogeneous density of the upper fourth of the right lung, which could perfectly well have been a pulmonary infarct, and apparently a decrease in vascular markings in the remainder of the right lung, a picture that has been described as typical of a large embolism to the pulmonary artery. I do not know whether this has been borne out by the X-Ray Department here, but it certainly seems to make sense.

Despite various measures including oxygen and penicillin the patient died after having had a small hemoptysis, which I believe was probably caused by pulmonary infarction.

Dr. Wyman, could we see the x-ray films?

DR. STANLEY M. WYMAN: The heart appears as described, extending down a considerable distance toward the left apparently owing to left ventricular enlargement. The left auricle is not well seen, but it projects posteriorly and appears enlarged. The hilar vascular shadows are considerably increased in size, but the vessels in the lung fields themselves are certainly not prominent.

DR. MYERS: Do you see anything that looks like old pulmonary emboli or infarcts?

DR. WYMAN: There are several indefinite linear shadows, which could be small infarct scars — for example, one in the right-middle-lung field in the fourth interspace. The film taken at the bedside a week later shows this homogeneous massive density in the apex of the right-lung field, which is perfectly consistent with a huge infarct. It is hard to compare the vascular markings on the two sides because the left-lung field is poorly shown on the bedside film. Part of the apparent decrease in vascularity on the right could be due to collapse of the upper lobe and spreading of the vessels in the right lung. I cannot see the typical "cut-off" shadow in the right hilar vessels that is also supposed to be important in pulmonary thrombosis, but I think thrombosis is a very definite possibility.

DR. MYERS: I should think, then, that I might settle for the diagnoses previously given. I believe that by far the most common event would be a massive pulmonary embolism rather than pulmonary thrombosis. A pulmonary embolus of that size would be more likely to come from the legs than from the auricle. However, I am sure that pulmonary thrombosis is a possibility. The great surprise to me is that thrombosis does not occur more often in pulmonary vessels having arteriosclerotic changes, particularly if they are insulted by repeated pulmonary emboli. I suppose there is one other thing that I should add: that something will turn out to be wrong with the kidneys. I would guess they showed old emboli.

DR. DONALD S. KING: I should agree with the diagnosis, but of course I wonder about pneumonia here instead of infarction. Is there anything in the story of a chill at the onset? I think one would have to accept the fever and the high white-cell count on the basis of a large infarct.

DR. REED HARWOOD: It is a somewhat unusual location for an infarct.

DR. JACOB LERMAN: I would like to ask Dr. Myers if it would not be unusual for obstruction of the peripheral circulation to develop from emboli without much pain.

DR. MYERS: I am sure it would be more common to have pain. It may turn out that the patient simply had thrombosis of the vessels of the lower extremities. Since he had this perfect setup for emboli and since I think he had had emboli to his lungs and kidneys, emboli to the legs would fit into one picture a little more readily. I have seen patients who have presumably had small emboli to the lower extremities who did not complain of much discomfort.

DR. ALLEN G. BRAILEY: Emboli are not likely to produce so much fever, are they?

DR. TRACY B. MALLORY: Sometimes there is quite a bit of fever and a markedly elevated white-cell count.

DR. KING: Pulmonary infarcts of that size could do it.

CLINICAL DIAGNOSES

Rheumatic heart disease, with mitral stenosis.
Lobar pneumonia.
Pulmonary infarcts.

DR. MYERS'S DIAGNOSES

Rheumatic heart disease, with mitral stenosis and regurgitation.
? Aortic stenosis.
Massive embolism or thrombosis of right pulmonary artery.
Infarction of upper portion of right lung.
Auricular fibrillation.
Congestive heart failure.
? Infarction of kidneys.
? Old arterial emboli to legs.

ANATOMICAL DIAGNOSES

Rheumatic heart disease, chronic, with mitral and aortic stenosis.
Pulmonary embolism, right, massive, old, with progressive recent thrombosis.
Pulmonary infarction, right upper lobe.
Coronary sclerosis with multiple occlusions.
Chronic passive congestion.
Renal and splenic infarcts, multiple old.
Nephrosclerosis, mild.
Cholelithiasis and chronic cholecystitis.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The underlying disease here was rheumatic heart disease, with involvement of both mitral and aortic valves. The mitral valve was very definitely stenotic and showed a crescent-shaped, quite narrow opening. The cusps of the aortic valve were sclerotic, partially calcified and somewhat fused, and the valve looked as if it might have been incompetent as well as slightly stenotic. The heart was considerably hypertrophied, weighing 570 gm., and the right ventricular hypertrophy was to our eyes a little more prominent than the left. There was extensive coronary-artery disease, with an old occlusion of the left descending branch, and a more recent occlusion of the right coronary artery. There was no myocardial infarction. The pulmonary arteries showed a very high grade of atheroma, a common finding in mitral disease, and there was a large adherent thrombus in the main right pulmonary artery that was only partially occlusive until the division running to the right upper lobe was reached, with continued fresher and completely occlusive thrombi in all its branches. A large part of the right upper lobe was massively infarcted. I think, as Dr. Myers has suggested, that there was a progression of thrombosis distal to the old adherent embolus in this case. We found evidences of old embolism in the form of healed scars of infarcts in the spleen and kidney. There was a mild nephrosclerosis as well. There were a few microscopic foci of acute polymorphonuclear infiltration around some of the blood vessels in the heart and also in the adrenal cortex for which I have no adequate explanation. They could easily have been caused by a septicemia, but the *Staph. albus* blood culture in life was not convincing evidence of that and the blood cultures at post-mortem examination were sterile, so that we have to leave them unexplained. There was nothing that suggested any acute rheumatic process.

DR. MYERS: Were the legs examined?

DR. MALLORY: The leg veins were examined, and no thrombi could be found. There was a large thrombus in the left auricle and a clot in the right auricle, but that on microscopical examination was quite clearly a post-mortem clot and not a thrombus.

DR. MYERS: How about the arteries in the legs?

DR. MALLORY: We went as low as the popliteal arteries and were not able to express any clot from them.

DR. HARWOOD: Was there marked sclerosis of the popliteal arteries?

DR. MALLORY: Moderate.

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DICTATED MEDICAL MILLENNIUM IN POLAND

AT THE end of 1949 the Polish Research and Information Service, of New York City, released a thirty-page report on public health in Poland. This report seeks to establish the conclusion that the Polish people have achieved an optimal system in the field of public health in the short period since the war, with various statements offered in support.

Thus, Poland before the war "was one of the most backward of European nations in meeting health needs" with only 0.9 per cent of the national budget devoted to this field. During the postwar period the budget for public health is reported to have risen until, in 1949, it was 3.3 per cent of the total. The result is that public health now "mirrors the profound social changes that have taken place." Since, behind the iron curtain, the merits of these profoun d social changes are not debatable matters, no question about the merits of their mirror image in medicine is permitted. The Polish people must accept the principle of Communism by force. The American people must accept the record of its accomplishments on the basis of reports given out through the ticket window in the iron curtain.

The system of compulsory health insurance in a people's democratic dictatorship "covers all employees no matter how high their income," and the bill for physicians, hospitalization and medication is paid entirely by the employer. This is to be contrasted with the situation before the war when "of the 84 per cent of the population not covered by health insurance, only a small number of well-to-do people could afford medical care." Inasmuch as the small number of well-to-do employers undoubtedly has decreased as the result of the war and the leveling process of sovietization, it is not quite clear how employers now foot all medical bills, for all workers, no matter how high their incomes.

The enviable status of motherhood, especially for the working woman, is evidenced by the policy that pregnant women are entitled to twelve weeks' leave with pay, eight of which must be taken after confinement. Their children may find health and happiness at resorts that, before the war, were "almost exclusively populated by children of wealthy parents." The reader of the *Polish Bureau of Information Bulletin* is not completely surprised to learn that "now the children of workers and farmers predominate. . . Rabka [one of the health resorts] is known popularly as 'the children's paradise.' "

Tuberculosis and venereal disease are reported to be declining in postwar Poland, where, to realize the principle of socialized medicine, doctors are required to devote forty-two hours weekly to public-health service on a salary basis. This regimented devotion of the doctors assures "the ambitious goal of building a socialist public health system." With prostitution no longer licensed, social inequalities no longer tolerated, mothers protected, children carefully nurtured and workers insured, a millennium of public health has indeed been inaugurated in Poland. One thorn only is permitted to be glimpsed among the rose blossoms, the lack of crystalline penicillin.

This is the responsibility of western capitalism, "because the United States refused to sell Poland equipment necessary for the production of crystalline penicillin."

Any comment on this report will doubtless be scrutinized more carefully by party than by public-health officials in an attempt to evaluate the efficacy of the work being performed by the Polish Research and Information Service. Actually, no comment on the status of public health in Poland can be made on the strength of this report except that the Research and Information Service has done its task faithfully and well — perhaps a little too well. American physicians will reserve interpretation until they can gain more than peephole glimpses through the iron curtain. They will await objective presentation of more facts by Polish physicians who have kept alive the spirit of scientific inquiry during two of the stormiest centuries ever weathered by a gallant nation. They will remember the tragic political background against which one of the greatest world scientists struggled at the beginning of this century in her quest for knowledge of radioactivity, even as they are aware that again Polish patriots are in rebellion against dictation.

QUALITY OF MEDICAL CARE IN A NATIONAL HEALTH PROGRAM

THE American Public Health Association adopted in 1944 a general statement of policy regarding medical care in a national health program. Such a program, according to this statement, should have as one of its basic objectives an insurance "that the services provided be of the highest standard and that they be rendered under conditions satisfactory both to the public and to the professions." In the fulfillment of such conditions all serious controversy over the distribution of medical care would obviously cease since no occasion for any further major differences of opinion could possibly exist.

As a result of the issuance of this statement a definition of medical care of high quality became necessary. This the Subcommittee on Medical Care of the Association, under the chairmanship of Dr. Dean A. Clark, has provided in a further statement recently made available in pamphlet form.* These objectives are defined to include promotion of positive health; prevention of disease, disability, and attendant economic insecurity; cure or mitigation of disease; and rehabilitation of the patient.

No proponent of free enterprise can quarrel with these objectives, and the remainder of the subcommittee's report is taken up largely with their definition and development in detail.

Much space accordingly is given over to a discussion of the procurement and training of various types of personnel, and to the problems of undergraduate and postgraduate medical education including uniformity in licensure of physicians and the periodic review of the qualifications of practitioners.

In the development of hospital standards regional co-ordination is stressed. The idea of the open hospital staff is encouraged, but with the restriction and supervision of practitioners' activities, as provided in the Gallupe Plan; full-time hospital staff nuclei are approved, as is the periodic medical audit, by the entire staff, of the quality of work that is being done.

It is in the matter of financing that the greatest difficulty would be encountered in making all eyes see as one, for the American Public Health Association is apparently committed to the principle that a national medical care program must be financed through social insurance supplemented by general taxation, or by general taxation alone. However, since it is also committed to the principle that the services provided be rendered under conditions satisfactory to the professions, the physicians of the country may rest assured that the Association will not exert its influence other than according to their desires.

Unquestionably, the advocates of tax-supported medical care honestly believe that service of a consistently high quality can be furnished to all segments of the population at a reasonable cost. They must believe also that this method of distributing and financing medical service will not continue beyond a generally acceptable limit, and that the

*Subcommittee on Medical Care. Quality of medical care in national health program. *Am. J. Pub. Health* **39**:898-924, 1949.

evolution of a democracy into a service state will not continue until many personal liberties have been suspended.

The honest opponents of a national tax-supported health program, on their part, want proof that such a plan will not deteriorate into a system of politically controlled medical practice.

Overfearful, perhaps, they still require some sign that man's capacity for political leadership has really risen to the point where honesty and intelligence will remain constantly at the helm, before they relinquish the checks and balances, clumsy as they are, that a system of individual enterprise provides. It appears to many that there is as yet no better sign than there has ever been that mediocrity, indifference and extravagance will no longer be factors in a system based on bureaucratic control.

MEDICAL LIBRARY ASSOCIATION

THE forty-ninth annual meeting of the Medical Library Association, which has become very active in the promotion of medical librarianship, both at home and abroad, will be held in Boston, June 19-23, with the Boston Medical Library as host. The primary membership of the Association is composed of medical and allied libraries, now numbering over three hundred and fifty, with two other important classes of members, supporting and professional. The former is open to all physicians and other persons interested in the promotion of medical and allied libraries and the organization of medical literature. The latter is limited to persons actively employed in medical and allied libraries.

The Association was organized in 1898 under the sponsorship of Dr. George M. Gould, the noted ophthalmologist and editor. Seven medical libraries were represented at the first meeting, held in Philadelphia, among them the Boston Medical Library. Dr. James R. Chadwick, the librarian, was unable to attend the meeting, but sent the assistant-librarian, Dr. Edwin H. Brigham, to represent the Library in his place, and young James F. Ballard was left at home to mind the Library.

Among the primary objectives proposed by Dr. Gould at the organizational meeting was the fostering of the exchange of medical literature between physicians and libraries. This activity began almost at once and has continued throughout the years of the Association, attaining large proportions.

The Association, as early as 1924, became interested in the international aspect of medical librarianship, and this activity has grown by leaps and bounds until today it is one of the great interests and activities of the Association.

The Association has its own *Bulletin*, published continuously since 1911.

The June meeting will feature a number of interesting events. Mr. William J. Bishop, librarian of the Wellcome Historical Medical Library, of London, will give the opening address entitled "Medical Libraries and Medical Librarianship in Great Britain." Dr. Merrill Moore, the well known Boston physician and poet, will be the principal speaker at the annual banquet. During the last few years, the Association has sponsored fellowships for foreign librarians for the purpose of studying medical libraries in the United States. The three current Fellows will report to the meeting. There will be a symposium on the important topic, "Historical Source Material of All Classes in All Types of Medical Libraries," with well known speakers from Boston, New York, Philadelphia, Salt Lake City and Washington. There will also be a symposium on technical methods of cataloguing, classification and indexing of medical literature, participated in by eminent librarians.

The first day will be devoted to visits to Harvard libraries in Cambridge, the new Massachusetts Institute of Technology Library, the Harvard Medical School and the Massachusetts General Hospital and its ether dome.

A hearty welcome is extended to the Association on the occasion of its annual meeting. Its accomplishments in the field of medical librarianship merit the respect of members and nonmembers alike. It is hoped that the Association will enroll supporting members, at the nominal dues of $5 a year, in numbers sufficient to guarantee that its valuable activities will be continued.

LYNN'S HOSPITAL PROBLEM

THE city of Lynn, with 1.3 acceptable hospital beds per thousand population, compared with a national standard of 4.0, finds itself on the horns of what should be a most uncomfortable dilemma.

The area is now served by two voluntary hospitals, the Lynn Hospital and the Union Hospital, which, with the addition of the 50 beds in the city infirmary and 20 in the Saugus General Hospital, give Greater Lynn a total bed capacity of 375. Of the 251 beds in the Lynn Hospital, however, 107 have been declared nonacceptable by the Massachusetts Department of Public Health "because of obsolete or non-fireproof construction"; all the 50 beds in the Union Hospital and all the 20 beds in the Saugus General have been similarly classified.

The 143,500 residents of Greater Lynn have thus 194 acceptable beds at their disposal!

Already the Union Hospital has started its campaign for funds to replace its present antiquated wooden structure with a modern 108-bed general hospital capable of expansion to accommodate 150 patients in an emergency. Of necessity the Lynn Hospital, with 107 nonacceptable beds, must soon broadcast its own appeal. If the first campaign — that for the Union Hospital — falls short of its goal and history repeats itself, the other will almost certainly fail.

A survey of the hospital requirements of Greater Lynn made recently by Dr. Gerald F. Houser, administrator of the Faulkner Hospital and secretary of the Massachusetts Hospital Association, pointed out the need for an over-all program of hospital development, and the wisdom of a united hospital campaign for funds.

The Union Hospital, struggling to meet its obligations in the community, must be given a new plant, but the welfare of the citizens of the area, which includes Lynn, Lynnfield, Nahant, Saugus and Swampscott, requires them to take a long view of the situation and heed the advice regarding cooperative effort.

No questions of local jealousy or pride in a particular organization should be allowed to obscure the issue. Where the needs of the community must be served by both institutions the only competition to be tolerated is that in the quality of such service.

PRIZE ESSAY

THE *Journal* is pleased to announce that the paper on poliomyelitis by Miss Ellen Vogel, fourth-year student at the College of Medical Evangelists, Loma Linda – Los Angeles, California, has been selected for the first prize of $100 in the 1950 prize-essay competition. Miss Vogel's essay is printed as the Medical Progress report in this issue of the *Journal*. The second prize, a two-year subscription to the *Journal*, was awarded to Mr. John G. Wells, a member of the graduating class at Johns Hopkins University School of Medicine.

Papers submitted for the 1951 contest should consist of a report of a case personally studied by the student submitting the essay, in combination with a discussion of the pathologic condition represented by the case and a review of the literature. The report, in general, should follow the form of case reports previously published in the *Journal*. Otherwise, the rules are the same as those stated for the 1949 and 1950 competitions:

> Manuscripts are to be not more than five thousand words in length, clearly typewritten in English, double or triple spaced with references listed at the end in numerical arrangement according to the form used by the *Quarterly Cumulative Index Medicus*. They must be in the hands of the editor by March 15, 1951, and must be accompanied by a certification from the dean of the medical school concerned stating that the author is a member in good standing of the fourth-year class and specifying the expected date of graduation. All manuscripts will become the property of the *Journal*.
>
> A cash prize of $100 will be paid for the best essay of those found to be suitable for consideration; the paper will be published in the *Journal* if the quality is considered to conform to the standards by which the editors judge material submitted, and the author will receive a hundred free reprints.
>
> A second prize will consist of a two-year subscription to the *Journal*.
>
> The editors wish to emphasize that in establishing this competition they are as much interested in encouraging good medical writing as they are in promoting the collection of scientific material. In judging papers that may be submitted, particular attention will accordingly be paid to clarity, simplicity and general literary excellence.

The history of medicine, from antiquity to the present time, certainly furnishes matter enough for the historian to speculate upon, for there is probably no other science wherein there has been so much diversity of opinion, so much scepticism and superstition manifested, as in medicine, from the remotest age. . . A century hence, our posterity will, without doubt, comment upon and review our proceedings in like manner, and will smile at many of our speculative theories and absurdities.

Boston M. & S. J., *June 5, 1850*

MASSACHUSETTS MEDICAL SOCIETY

SOCIETY EXHIBIT

The Massachusetts Medical Society will sponsor an exhibit at the fourth annual Massachusetts Public Health Conference to be held at the University of Massachusetts in Amherst on June 14, 15 and 16.

The exhibit, made of masonite, depicts on three panels the many and varied activities of the Society. Designed to inform the general public of the services of the Society, it lists and illustrates the following: postgraduate training; the *New England Journal of Medicine*; support of the Boston Medical Library; working committees; co-operation with city, state, county, national and private health agencies; Woman's Auxiliary; information service for fellows; public information; awards; and promotion of voluntary health insurance.

The Massachusetts Public Health Conference is sponsored by the Massachusetts Public Health Association, Massachusetts Department of Public Health, University of Massachusetts and New England Health Institute.

POSTGRADUATE EDUCATION OF PHYSICIANS

The Committee on Postgraduate Medical Education of the Society has completed another excellent year. The report presented at the Council meeting on May 15 should be a matter of pride to the fellows and of proper satisfaction to all concerned with this important work.

The various programs and exercises are designed primarily for the general practitioner. It is further emphasized that the programs are offered without cost. All physicians are invited to participate, whether they are fellows of the Society or not.

This is an important point, since approximately a fourth of the licensed physicians of the Commonwealth are not members of the Society. The problem of new graduates from substandard schools has been eliminated. A large number of unassimilated graduates from such schools remain in practice. Efforts to offer such graduates the opportunity to meet ethical and professional requirements for fellowship should be encouraged.

Many such graduates remain unaware of the teaching facilities offered by the Society. It is urged that fellows of the Society and particularly those arranging programs in the districts make the meetings known as widely as possible.

DEATHS

BEAN — Harold C. Bean, M.D., of Salem, died on May 21. He was in his fifty-ninth year.

Dr. Bean received his degree from Harvard Medical School in 1918. He was a member of the Boston Orthopedic Club and a fellow of the American Academy of Orthopaedic Surgeons and the American Medical Association.

His widow, his mother and two daughters survive.

HIGGINS — Frank A. Higgins, M.D., of Newton, died on January 3. He was in his eighty- fifth year.

Dr. Higgins received his degree from Harvard Medical School in 1893.

Two sons survive.

KELLEY — Clarence M. Kelley, M.D., of Melrose, died recently. He was in his sixty-sixth year.

Dr. Kelley received his degree from Harvard Medical School in 1910. He was a member of the American Psychiatric Association.

A son and a daughter survive.

MADDEN — William D. Madden, M.D., of Boston, died on May 17. He was in his eighty-second year.

Dr. Madden received his degree from Harvard Medical School in 1894. He was a former member of the staffs of the Massachusetts Eye and Ear Infirmary and the Boston City Hospital and was a fellow of the American Medical Association.

Two sisters survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

OFFICE HOURS

The various divisions and sections of the Massachusetts Department of Public Health are open regularly from 8:45 a.m. to 5:00 p.m., Monday through Friday. Only emergency coverage is maintained on Saturdays, Sundays and holidays. The office of the Capitol Police in the State House (CApitol 7-4600, Extension 208 or 209) is provided with a list of the Department personnel designated on call for emergency service.

There will be one member of the Biologic Laboratory staff on call for emergency orders for biologic products that cannot be filled from the various stations located in Boston and throughout the Commonwealth.

The Bacteriological Laboratory is open mornings on Saturdays, Sundays and holidays for the performance of urgent tests, and may be reached by telephone (JAmaica 4-5440) during these hours.

Emergency calls for other Department offices are handled by physicians designated for this emergency service. The calls directed to the Capitol Police are referred to the proper person.

BOSTON MEDICAL LIBRARY

WASSERMANN COLLECTION

The "hand-apparat" of this famous physician and investigator has been catalogued and made available for reference in the library. This collec-

tion is typical of the methodical German scientist, who gathered around him the small hand pieces, comprising the apparatus commonly used in his work; it consists of reprints, pamphlets per se, academic dissertations and small monographs, in contradistinction to the periodicals and books in his library.

The total number of items is 3923 by approximately 4000 authors. The author catalogue reads like a directory of eminent names in the fields of bacteriology and immunology, including Baginsky, Citron, Ehrlich, Lazarus, Levaditi, Leo Loeb, Metchnikoff, Neisser, Noguchi, Pfeiffer, Proskauer, Roux, Hans Sachs, Shiga, Uhlenhuth and Wolff-Eisner. There are a large number of Wassermann's reprints. Many of the pieces are inscribed or autographed copies.

August von Wassermann (1866–1925) studied in various German universities and began the practice of medicine in Strassburg in 1888. He joined the staff of the Robert Koch Institute for Infectious Diseases in Berlin and in 1906 became head of the department of experimental therapy and serum research. In 1913 he became director of the Kaiser Wilhelm Institute in Berlin. In 1907 he made his discovery of the serodiagnostic test for syphilis, commonly called the Wassermann reaction.

CORRESPONDENCE

MINORITY REPORT ON CASH SICKNESS COMPENSATION

To the Editor: For the information of the Fellows of the Massachusetts Medical Society I am forwarding a condensation of my report submitted to the Legislature. This report was drafted as a result of investigation while I was serving on the Massachusetts Recess Commission on Cash Sickness Compensation, created by Chapter 63 of the *Resolves* of 1949, to study the problem implied in its name, and to recommend to the General Court of 1950 such legislation as it deemed advisable. The condensation is as follows:

I have kept uppermost in my mind the conditions recited by the Governor in his address of July 21, 1949, in which he pointed out that the Commonwealth, by its Workmen's Compensation Law, protects the man who loses work as result of an accidental injury or an occupational disease; that the Commonwealth, by its Employment Security Law, insures the payment of unemployment compensation benefits to the family of the breadwinner who loses his job by termination, a shutdown, a layoff or other economic causes beyond his control; but that there is no provision for protecting or insuring employees and their families against an equal, if not a greater hazard — that which arises from nonindustrial injury and nonoccupational sickness.

As a member of the medical profession and as a citizen of the Commonwealth, I dissent most vigorously with the portion of the report of the majority that recommends the establishment of a monopolistic state fund for providing these benefits.

I hold to the view that "that people is best governed which is least governed," that Government exists for the people and not the people for the Government, that Government activity should be confined to "regulation" and should extend to "control." I hold to the views that Government should provide for the greatest good of the greatest number, that our country was made and became great through "free enterprise," which is the antithesis of Communism. Adhering to the American tradition, I am of the opinion that Government should not enter into the field of private insurance until those authorized by law to transact insurance business under our laws are unable or unwilling to meet the challenge and to discharge their responsibilities. Our insurance laws, enacted and perfected by the state government over a long period of years, were designed to ensure the good and welfare of the Commonwealth, and if, and so long as, persons are given the right and charged with the responsibilities of providing insurance under those laws and are properly regulated, that the system under those laws should be supported and maintained. Those laws were designed, among other purposes, to provide an answer to the problem under consideration.

In the light of the foregoing, of that which I have heard and learned in the hearings held by the Commission and from my own personal study, I submitted a bill for the consideration of the General Court. The purposes of the bill are fully set forth in its first section. In general, its provisions are consistent with the views I have expressed herein and with the principle of private enterprise in establishing a system of compulsory insurance to guarantee payment of the benefits it provides; it affords the right to certain employers to become self-insurers if they so choose by furnishing adequate security; it affords the right to employers who are required to insure, but who cannot obtain insurance, nevertheless to obtain insurance under a system authorizing the Commissioner of Insurance to assign rejected risks equitably among all insurance companies. It does not disrupt existing plans of health and accident insurance under which some employers now provide the whole cost, or the cost with contributions from employees, provided, however, that such plans furnish benefits at least as favorable as those required by the bill, if it shall become law; it provides for such new plans as are approved; and last and most important, it provides these benefits while the employee is deprived of earning through nonoccupational injury or illness, whether occurring while his employment continues or while he is unemployed, and to that extent, covers the present twilight zone in which an employee so deprived is not entitled to benefits under either the Workmen's Compensation Law or the Employment Security Law.

MATTHEW V. NORTON, M.D.
122 Commonwealth Avenue
Boston

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

More About Psychiatry. By Carl Binger, M.D. 8°, cloth, 201 pp. Chicago: University of Chicago Press, 1949. $4.00.

In this small volume Dr. Binger presents a series of fourteen essays intended for the physician and interested layman. They fall naturally into several general groups: psychosomatic medicine, on the relation of medicine to psychiatry, psychiatry and the relation of the individual to the community and to the general world situation. There is a topical bibliography and a good index. The book is well published.

Immunizacion contra el tifus exantematico con vacuna viva, cepa e. By G. Clavero del Camp, director of the Escuela Nacional de Sanidad; and Dr. F. Perez Gallardo, physician of the Escuela Nacional de Sanidad. 12°, paper, 102 pp., with 28 illustrations. Madrid: Gráficas González, 1949.

The first two chapters of this small monograph give in detail laboratory experiments on animals, for the purpose of ascertaining the possibility of immunization against typhus by the use of a live virus, strain E of *Rickettsia prowazeki.* The third chapter discusses its use in human beings. There are a comparatively large number of charts and tracings. The monograph is number twenty-six in a series, *Colección de folletos para médicos, sobre temas de carácter sanitaria,* published by the Dirección General de Sanidad. The complete series, which is well published, is interesting and should be available in all large medical libraries.

The Cry and the Covenant. By Morton Thompson. 8°, cloth, 469 pp. Garden City, New York: Doubleday and Company, Incorporated, 1949. $3.50.

This novel describes the scientific life of Dr. Ignaz Philipp Semmelweis and his combat with puerperal fever. His trials and tribulations are faithfully portrayed in a dramatic manner. The novel should be in all medical-history collections.

Nutritional Data (formerly "Nutritional Charts"). Compiled by Harold A. Wooster, Jr., and Fred C. Blanck. 8°, paper, 114 pp. Pittsburgh, Pennsylvania: H. J. Heinz Company, 1949. Gratis.

This volume is made up to a large extent of a great many tables and charts. The text treats in order the vitamins, the essential nutritional elements, proteins and amino acids, the availability of nutrients, signs and symptoms of malnutrition, the metabolism and action of foods, human nutritive requirements, diet planning and tables of food composition and nutritive value. The text is well printed and should prove very useful to all persons interested in dietetics.

A Candle in Her Hand: A story of the nursing schools of Bellevue Hospital. By Dorothy Giles. 8°, cloth, 240 pp., with 18 illustrations and frontispiece. New York: G. P. Putnam's Sons, 1949. $4.00.

In this book the author first treats of the early history of nurses and nursing services, and hospitals in New York City from 1643 to 1811. This is followed by chapters on New York's first trained nurses and seventy-five years' progress of nursing in Bellevue Hospital. The text is well written, and the book is well published. It should be in all collections on the history of nursing.

The Vitamins in Medical Practice. By J. Shafar, M.D., M.R.C.P., D.P.H. 8°, cloth, 383 pp. New York: Staples Press, 1949. $4.50.

The early chapters of this book are devoted to a discussion of the chemistry, physiology and deficiency conditions of the various well known vitamins. These are followed by chapters on beriberi, pellagra, scurvy and rickets. The concluding chapters treat of the vitamins in disorders of the various systems and organs of the body. A bibliography of over 1800 references concludes the text, and there is a good index. The book was printed in England and is well published. It should be in all medical libraries and should prove valuable to persons interested in the subject.

A Short History of Physiology. By Kenneth J. Franklin, D.M., F.R.C.P., professor of physiology at the Medical College of St. Bartholomew's Hospital. Second edition. 8°, cloth, 147 pp., with 16 illustrations. New York: Staples Press, 1949. $2.00.

This second edition of a small book first published in 1933 has been revised to include additional information gathered by the author during the intervening years. The period covered is from the time of the rise of physiology in the ancient world to the nineteenth century. The book is well published in every way. The material has been recast, and the volume published in a new, attractive format. Sixteen illustrations, consisting of full-page plates, have been added to this edition. There is an index of personal names. The text is well written and well arranged. A good large type has been used, and the paper is soft, without glare, making for easy reading. The book is recommended to all persons interested in the subject and to medical libraries.

NOTICES

POSITIONS AS MEDICAL OFFICER AT ST. ELIZABETHS HOSPITAL

The United States Civil Service Commission has announced examinations for positions of medical officer (rotating intern and psychiatric, surgical and general-practice resident) in St. Elizabeths Hospital, Washington, D. C.

Salaries for rotating intern are $2200 the first year and $2400 the second year; for psychiatric resident and general practice resident, from $2000 to $4150 a year; and for surgical resident, from $3400 to $4150 a year. To qualify for these positions, applicants must have had appropriate education in an approved medical school. Applicants for positions of psychiatric, surgical and general-practice resident must also have completed a one-year internship. In addition, applicants for surgical-resident appointments must have completed a three-year residency in surgery. No written test will be given.

Further information and application forms may be obtained from most first-class and second-class post offices, from Civil Service regional offices or from the United States Civil Service Commission, Washington 25, D. C. Applications will be accepted until June 20, 1950, by the Committee of Expert Examiners, St. Elizabeths Hospital, Washington 25, D. C.

MEDICAL LIBRARY ASSOCIATION

The annual convention of the Medical Library Association will be held in Boston, June 19-22. The Boston Medical Library will be host, and hotel headquarters will be at the Hotel Kenmore.

An address on "Medical Libraries and Librarianship in Great Britain" by Mr. William J. Bishop, Librarian of the Wellcome Historical Medical Library, London, will be one of the outstanding lectures at the meeting. The "Symposium on Historical Source Material in Medical Libraries" and conducted visits to the libraries of Harvard, Massachusetts Institute of Technology, Massachusetts College of Pharmacy and the Massachusetts General Hospital will be of special interest to all medical and scientific librarians.

PLASTIC-SURGERY AWARD

The Foundation of the American Society of Plastic and Reconstructive Surgery offers as its 1950 award $500 (first prize of $300, second prize of $200) and a certificate of merit, for essays on some original unpublished subject in plastic surgery. Competition is limited to residents in plastic surgery in recognized hospitals and to plastic surgeons who have been in such specific practice for not more than five years.

The first prize essay will appear on the program of the forthcoming annual meeting of the American Society of Plastic and Reconstructive Surgery, to be held in Mexico City, November 27-29. Essays must be submitted before August 15, 1950.

Full particulars may be obtained from the Secretary, Dr. Clarence R Straatsma, 66 East 79th Street, New York, New York.

SOCIETY MEETINGS AND CONFERENCES

JANUARY 9-DECEMBER 1. Laboratory Courses at Communicable Disease Center, Atlanta, Georgia. Page 950, issue of December 8.

JUNE 12-14. American Neurological Association. Page 600, issue of April 13.

JUNE 13. New England Society of Anesthesiologists. Page 735, issue of May 4.

JUNE 13. South End Medical Club. Page 886, issue of June 1.

JUNE 14-16. New England Health Institute and Massachusetts Public Health Conference. Page 768, issue of May 11.

JUNE 19-22. Medical Library Association. Notice above.

JUNE 20, 22 AND 23. Springfield Hospital. Page 848, issue of May 25.

JUNE 22-25. American College of Chest Physicians. Page 270, issue of February 16.

JUNE 23 AND 24. International Academy of Proctology. Page 768, issue of May 11.

JUNE 24 AND 25. American Society for the Study of Sterility. Page 38, issue of January 5.

JUNE 24 AND 25. American Academy of Dental Medicine. Page 640, issue of April 20.

JUNE 25. Western Association of Industrial Physicians and Surgeons. Page 886, issue of June 1.

JUNE 26-30. American Physicians Art Association. Page 428, issue of March 16.

JUNE 26-30. American Medical Association. Annual Session. San Francisco, California.

JULY 2-5. American Proctologic Society. Page 848, issue of May 25.

JULY 3. Brazilian Society of Cardiology. Page 886, issue of June 1.

JULY 17-22. International Congress for Scientific Research. Page xvii, issue of September 1.

(*Notices concluded on page xix*)

NOTICES *(Concluded from page 922)*

AUGUST 21–26. International Society of Hematology. Page 888, issue of December 1.

AUGUST 28–SEPTEMBER 1. American Congress of Physical Medicine. Page 428, issue of March 16.

AUGUST 31–SEPTEMBER 7. World Federation for Mental Health. Page 306, issue of February 23.

SEPTEMBER 3–9. International Heart Congress. Page 160, issue of January 26.

SEPTEMBER 27–29. Mississippi Valley Medical Society. Page 991, issue of December 15.

OCTOBER 12–14. American Association of Blood Banks. Page 428, issue of March 16.

NOVEMBER 1. New England Obstetrical and Gynecological Society. Hotel Somerset, Boston.

JANUARY 31. American Academy of Orthopaedic Surgery (see Kappa Delta Award for Research in Orthopedic Surgery). Page 736, issue of May 4.

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, JUNE 15

FRIDAY, JUNE 16

*9:00 a.m.–12:00 m. Combined Medical and Surgical Staff Rounds. Peter Bent Brigham Hospital.

*1:30 p.m. Tumor Clinic. Out-Patient Department. Mount Auburn Hospital, Cambridge.

MONDAY, JUNE 19

Medical Library Association, Boston Medical Library.

*11:30 a.m.–12:15 p.m. Chest X-Ray Conference. South End Health Unit, 57 East Concord Street, Boston. Dr. Cleaveland Floyd in charge.

*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.

TUESDAY, JUNE 20

Medical Library Association, Boston Medical Library.

*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.

*1:30–2:30 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.

WEDNESDAY, JUNE 21

Medical Library Association, Boston Medical Library.

*11:00 a.m.–12:00 m. Medical Rounds. Children's Medical Center.

*12:00 m. X-Ray Conference. Margaret Jewett Hall, Mount Auburn Hospital, Cambridge.

*12:00 m.–1:00 p.m. Clinicopathological Conference (Children's Medical Center). Amphitheater, Peter Bent Brigham Hospital.

*2:00–3:00 p.m. Combined Clinic of all Medical Center Services. Amphitheater, Children's Hospital.

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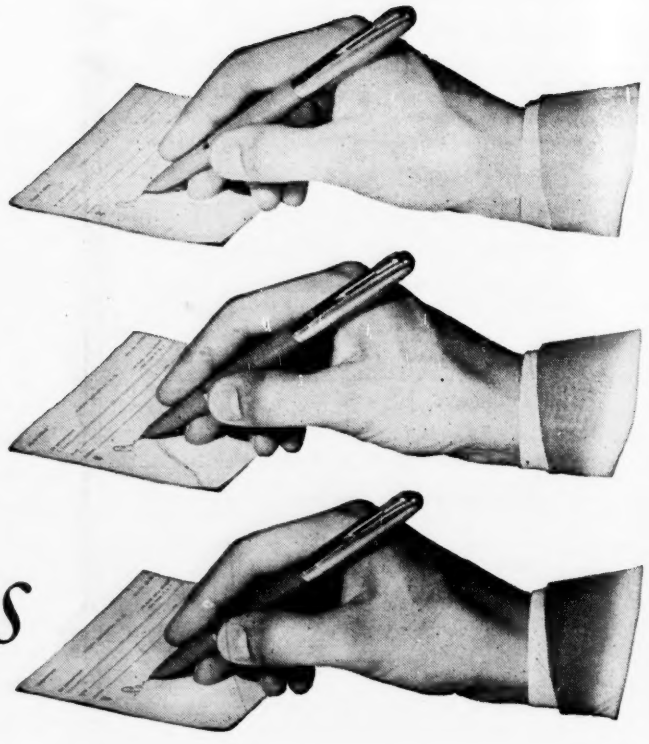

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